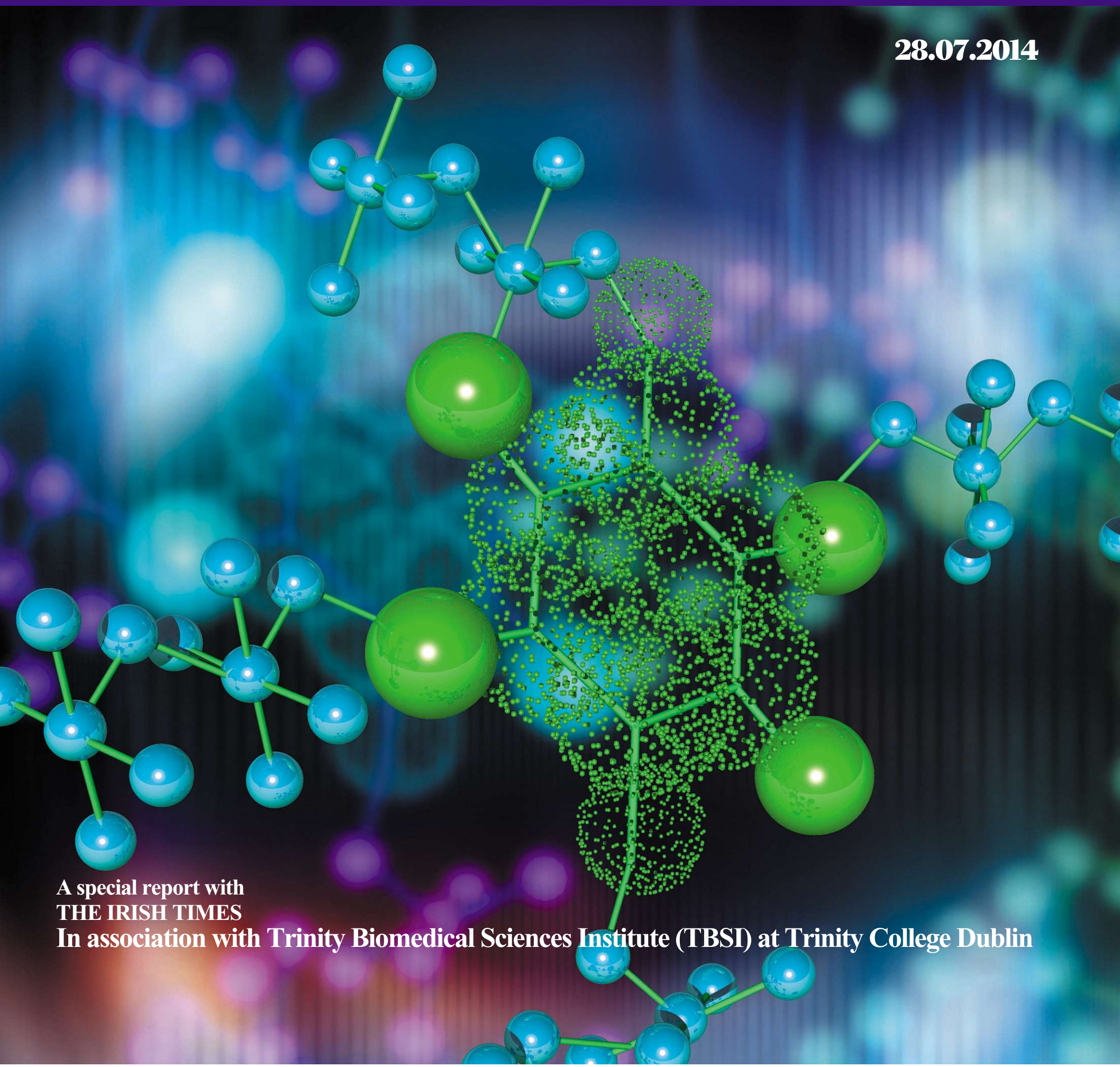
CUTTING EDGE RESEARCH
IN CANCER AND IMMUNOLOGY



28.07.2014

A special report with
THE IRISH TIMES
In association with Trinity Biomedical Sciences Institute (TBSI) at Trinity College Dublin

TRINITY COLLEGE DUBLIN
COLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH
THE UNIVERSITY OF DUBLIN

Trinity Biomedical Sciences Institute

Over the last 20 years biomedical research has grown strongly in Trinity College Dublin with particularly strong growth in output after 2000, resulting in a high international standing. In 2006, a detailed review of Trinity's biomedical research activities was conducted by Nobel Laureate (1996) Prof Peter Doherty of the University of Melbourne and Prof Sir Stephen O'Rahilly, currently Professor of Clinical Biochemistry and Medicine at the University of Cambridge. The reviewers concluded that:

'A free-standing "Trinity Biomedical Sciences Institute"...should be on the Trinity main campus...(with a) function to support translational research...'.

This recommendation formed the basis of the development of the Trinity Biomedical Sciences facility which consolidates and co-locates pre-clinical bioscience research activities across five schools – Chemistry, Engineering (Bioengineering), Biochemistry & Immunology, Medicine and Pharmacy & Pharmaceutical Sciences. The development generates a meaningful consolidation of Trinity's complementary biomedical research activities under the one roof and co-location facilitates the achievement of the close interdisciplinary collaboration required for 21st Century biomedical research. The facility integrates and scales three interlinked proven quality research themes, Immunology, Cancer and Medical Devices, in a single facility, and underpins and links to translational research at the Trinity Centre in St James's Hospital incorporating the Institute for Molecular Medicine and the Wellcome Trust Clinical Research Facility on that site.

Instrumentation

Within the facility, core instrumentation is available to support researchers from Trinity, other Colleges and industry. Available state-of-the art instrumentation is extensive and includes:

- 800MHz Nuclear Magnetic Resonance Spectrometer – contact Matteo Pennestri , PENNESTM@tcd.ie
- 400MHz Nuclear Magnetic Resonance Spectrometer – contact Manuel Ruether, RUETHERM@tcd.ie
- Transmitting Electron Microscope – contact Derek Nolan, DENOLAN@tcd.ie
- Confocal Microscopes including Super Resolution down to 50nm – contact Gavin McManus, MCMANUG@tcd.ie
- Fluorescent Activated Cells Sorter (FACS) – contact Barry Moran, MORANBA@tcd.ie
- Flow Cytometers – contact Barry Moran, MORANBA@tcd.ie
- Mass Spectrometers – contact various, enquiries to Tony Byrne, tony.byrne@tcd.ie
- XRay crystallography machines – contact various, , enquiries to Tony Byrne, tony.byrne@tcd.ie
- Seahorse Respirometer – contact Richie Porter, RKPORTER@tcd.ie

Facilities

Research facilities are available to accommodate up to 700 researchers and support staff. Facilities are also available to support teaching, research seminars and conferences. These include:

- 2 x 300 seater lecture theatres
- 11 x seminar rooms with seating capacities from 20 to 105.

These are equipped with advanced AV and video-conferencing facilities and are bookable when not in use for teaching. Enquiries can be made by emailing Siobhan.McGurk@tcd.ie.

In addition to the above facilities the School of Biochemistry has a large Biochemistry teaching laboratory and the School of Medicine has state-of-the-art Anatomy and Physiology teaching laboratories.

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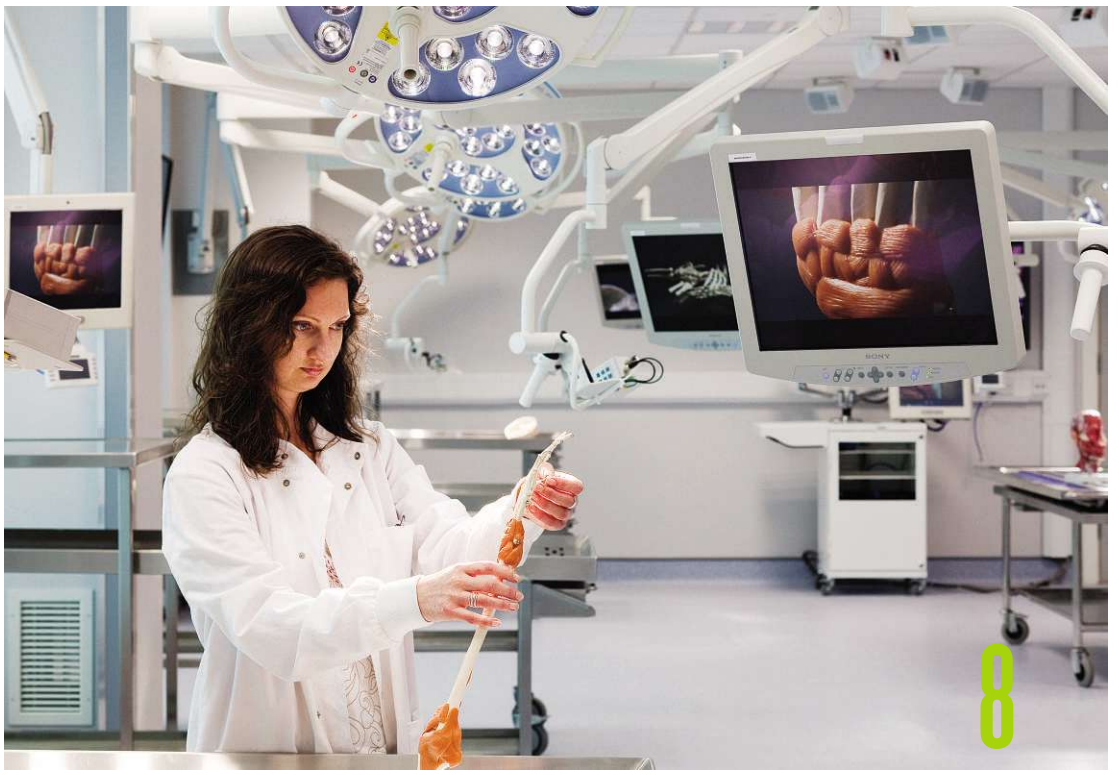
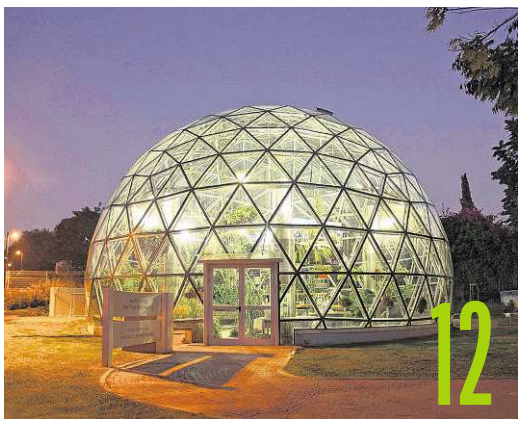
www.tcd.ie/biosciences

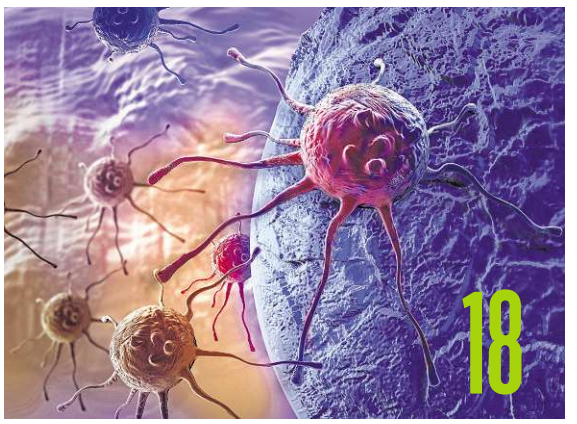
CUTTING EDGE RESEARCH

IN CANCER AND IMMUNOLOGY

INSIDE







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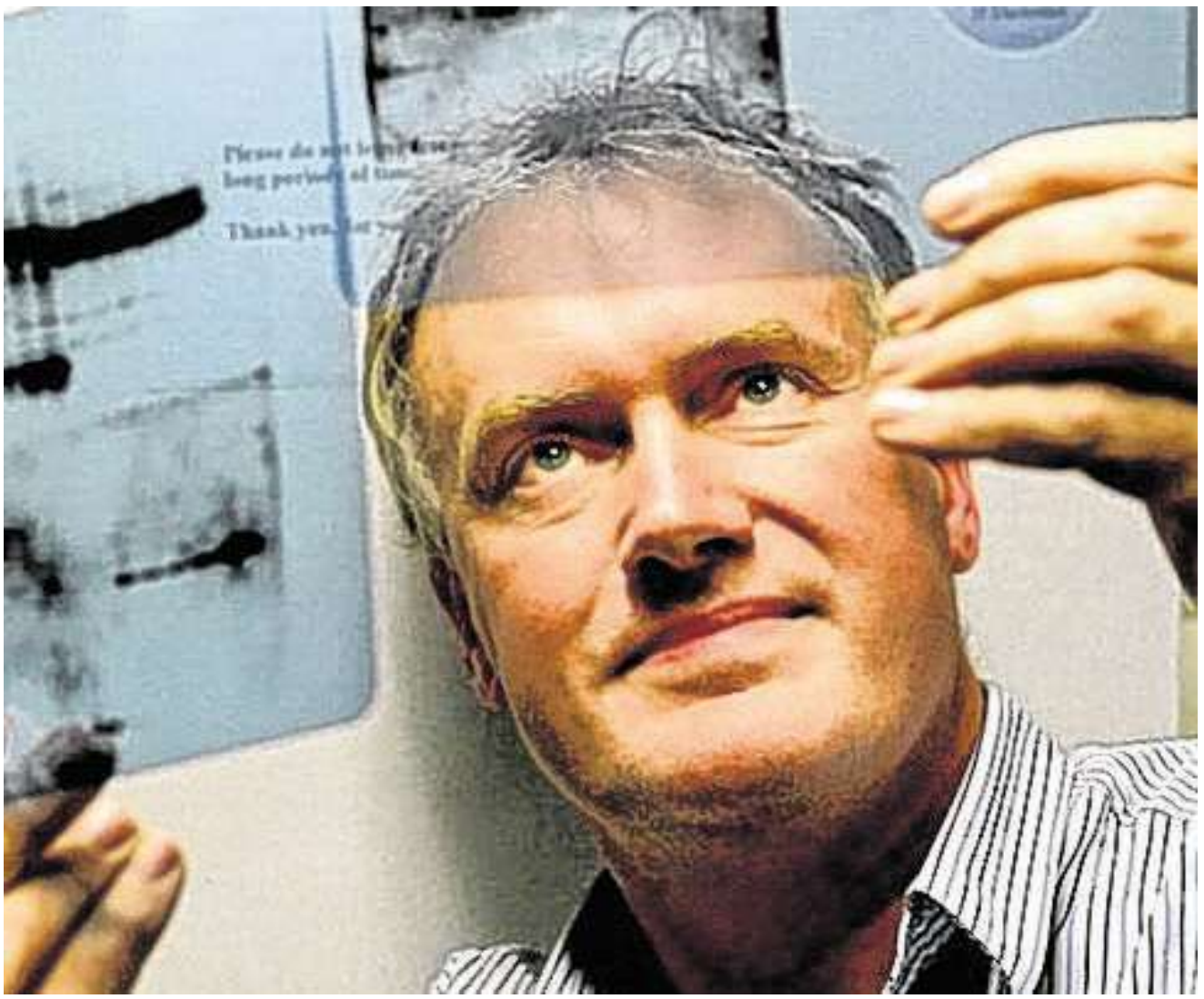
Scientists from around the world converge on Dublin

The conference is part of TBSI's mission to form relationships with other renowned institutes, writes **Prof Luke O'Neill**



I am delighted to welcome scientists from around the globe to Dublin and the Trinity Biomedical Sciences Institute (TBSI), to our very special inaugural meeting with friends and fellow scientists from the Weizmann Institute of Science. TBSI houses more than 500 scientists and clinicians in Trinity working on the major diseases that afflict humanity, including cancer, inflammatory diseases and neurological disorders.

We are also educating the next generation of doctors and scientists. Five schools came together in the largest movement of researchers in Trinity's history. Biochemistry and immunology, medicine, bioengineering, pharmacy and pharmaceutical sciences and chemistry all joined forces to form what is becoming an internationally recognised institute. TBSI is housed in a purpose-built facility on Pearse Street of 21,000sq m and we are very grateful to the Higher Education Authority PRTLI programme for providing key support. We are delivering real impact – scientific, educational, economic and societal.

Recent notable successes include the creation of 119 jobs funded from non-exchequer sources. These jobs are at the postgraduate and postdoctoral levels and are making contributions to our efforts at a very high level. We are working with 76 pharmaceutical, medical device and diagnostics companies. Our discoveries are being published in the world's leading journals and represent major advances in our understanding of diseases such as whooping cough, inflammatory bowel disease, eczema, motor neuron disease, sepsis and cancer. Our chemists and pharmacists are making new medicines, our bioengineers are making new medical devices to help patients and we are supporting spin-out companies such as Opsona Therapeutics and Trino to help commercialise our research. We are also collaborating with colleagues in UCD under the Innovation Alliance, which promotes entrepreneurship among our students. We hope that our discoveries will give rise to better patient care and we are working closely with colleagues in St James's Hospital to achieve that ultimate goal.

A key mission of TBSI is to form relationships with other renowned institutes and this is exactly what the meeting is all about. The idea for the meeting came about from informal discussions between me and Prof David Wallach,who holds the Joseph and Bessie Feinberg Chair at the department of biological chemistry of the Weizmann Institute of Science, at a conference in Italy. The idea mushroomed and we were delighted to include seven keynote speakers in our programme, five of whom are Nobel Laureates in medicine or physiology, and chemistry. We are honoured to host our visitors since the Weizmann Institute is what we aspire to be. It is one of the world's leading research institutes which has made major contributions in medicine. Millions of patients are benefitting from discoveries made in the Weizmann, notable examples being in diseases such as rheumatoid arthritis and multiple sclerosis. My co-organiser, David Wallach, did critical early work that led to the development of new drugs for arthritis. These drugs are being made by pharmaceutical companies in Ireland who are employing thousands of people, serving as an excellent example of how basic research can benefit both patients and the economy.

The Weizmann is a model for how government investment in research is paying off. It's a long-term game, however, requiring patience and commitment and we hope Ireland will hold its course in its undoubted commitment to funding scientific research. On the last day of the conference we will discuss how best to reap the rewards from research investment, with talks from Mark Ferguson, director of Science Foundation Ireland and chief scientific adviser to the Irish Government; Mudi Sheves, the Weizmann's vice-president for technology transfer and Diarmuid O'Brien, director of Trinity research and innovation. What are we hoping for? Collaboration, collegiality as scientists and friends, and ultimately great discoveries. Science is highly collaborative, where we can deploy each other's expertise to break new ground.

> "Our discoveries are being published in the world's leading journals and represent major advances in our understanding of diseases

I thank our distinguished external speakers, whose participation shows the commitment of scientists to make a difference. We aim to foster collaboration and encourage the up-and-coming generation – our students and postdocs – to join us on this endless and honourable journey.

Prof Luke O'Neill: delighted to welcome scientists from around the globe to Dublin

Prof Luke O'Neill is professor of biochemistry and TBSI academic director

Speed dating for scientists

The amiable collaboration of two experts in immunological research kick-started co-operation between TBSI and the Weizmann Institute, writes **Dick Ahlstrom**

A novel kind of speed dating will be happening at a conference at Trinity College Dublin which started yesterday and runs until Tuesday evening. But the participants won't be looking for romance; it will be about collaborating on scientific research.

The three-day meeting has attracted more than 500 top scientists from around the world including five Nobel Prize winners, all of whom will speak at the event, entitled: Medical Research at the Cutting Edge – Progress in the Fight Against Inflammatory Diseases and Cancer.

The twin emphases reflect two areas of research strengths shown by Trinity Biomedical Sciences Institute (TBSI) and the Weizmann Institute of Science, the two organisations who have teamed-up to make this an annual event on the scientific calendar.

"The whole beauty of science is collaboration," says Prof Luke O'Neill the academic director of TBSI and professor of biochemistry. "It will be a fancy kind of speed dating. We are hoping for lots of dialogue and interaction. It will be a free flowing event with the hope of getting collaboration going."

He organised the event with Prof David Wallach of the Weizmann Institute who also stressed the value of contact between scientists. "In science there is an importance to fraternity. We highlight the names of the big achievers like the five Nobelists, but science is done through co-operation with people from all over the world," he says. "You need to communicate – it leads to co-operation."

The meeting itself was prompted by contacts between O'Neill and Wallach who are both involved in very advanced immunological research. And it was not a high powered exchange in a lab but rather a conversation over a glass of wine.

"We were at a conference in Italy. David was president of the International Cytokine Society and I was incoming president and we knew each other well," says O'Neill. "The question came up of Israel and science and I said I didn't know much of what was happening in science there. He then suggested we hold a joint conference. What began as a chat over a glass of wine turned into this huge thing. They collaborate with Yale and Harvard so it is an honour they are coming here."

Wallach views the meeting as a springboard for greater co-operation between Irish and Israeli scientists. "There are already collaborations between scientists in Israel and in Ireland but it is very limited so the purpose of the meeting is to extend this," he says. "You can't impose it; we are telling students in Ireland to have a look and see if they want to visit any of the scientists at Weizmann."

For this reason the two institutes are also setting up a fund to support students and scientists who want to take part in a three-month exchange (see panel). "The idea is that this will be bi-directional," says Wallach. "This is a practical thing, but it is the basis of science."

O'Neill is familiar with the Weizmann Institute and what anyone spending time there might experience. "They have a very good entrepreneur programme there to tune up the students about the commercialisation of research."

In fact there are a number of sessions during the conference on this issue. "I hope we will learn from them how best to cap-

Meeting of great minds Five Nobel laureates, 500 scientists

There are those who are sceptical about the value of professional conferences but for those who know what they can deliver, they represent something else. When great minds come together, great things hopefully will emerge.

There will be plenty of great minds on hand at Trinity College Dublin tomorrow at a conference that no fewer than five Nobel laureates will address.

Each will deliver keynote addresses at the Trinity Biomedical Sciences Institute, but they will also be important as an inspiration for the young scientists who will be in attendance at the three-day event.

The real impact from the conference however will be what follows afterwards, suggests Prof Varda Rotter of the Weizmann Institute. "These conferences are very productive and initiate very good collaboration," she says. "The broad, basic idea is: lets collaborate."

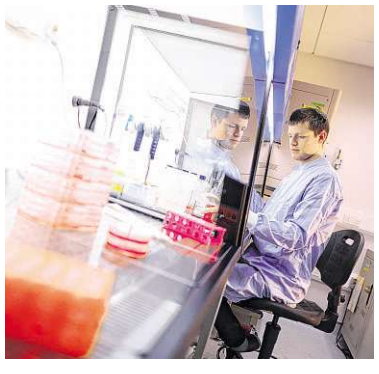
What follows is was also highlighted by the Trinity institute's academic director Prof Luke O'Neill. "My main hope is for great science to happen afterward. I think this will really lead to greater collaboration and we will see real research advances," he says.

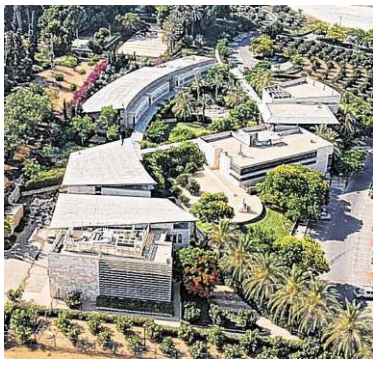
The Weizmann Institute's Prof David Wallach agrees. "In general, it is a precondition in science to have this kind of communication. And you can never really predict what will come of it," he adds.

Certainly there will be plenty of opportunity to communicate given that the numbers attending have topped 500 and there is almost more demand than there are places at the event.

And if all goes well there will be a repeat engagement with the Weizmann hosting a similar event next summer.

DICK AHLSTROM





Clockwise from far left: part of the Weizmann campus; research at TBSI; the submicron lab at the Weizmann Institute, where researchers develop semiconductor structures; aerial view of the campus in Rehovot, Israel; analysis at TBSI; and Trinity's facility on Pearse Street, Dublin

'Reciprocal exchange and joint tutorship' A memorandum of understanding

The symposium involving the Weizmann Institute of Science and the Trinity Biomedical Science Institute (TBSI) is the first in what it is hoped will be an annual event alternating between Dublin and the Weizmann Institute's base in Rehovot, Israel. But this is not the only item on the agenda.

The two institutes will sign a memorandum of understanding to explore the potential for collaboration in a number of research areas including cancer and immunology. The memorandum will also set up a "reciprocal exchange and joint tutorship" for graduate students and post doctoral researchers.

While the agreement is associated with the availability of funds, the initial plan is to support the travel of up to 10 students or scientists in total per year from both of the institutes via a newly formed travel support fund. The student or scientist will visit for periods of up to three months and have their travel costs, accommodation and living expenses covered.

When the Weizmann Institute hosts the next annual meeting, the students who travelled and the labs that hosted them will be offered a chance to make presentations related to the research they conducted.

The follow-on meeting at the Weizmann and the studentships that will come from the first annual conference represent a "legacy" aspect, says Prof Luke O'Neill of TBSI.

DICK AHLSTROM

ture the IP [intellectual property] from research. There is no question they are leading the world on this."

Wallach echoes this view. "The conference has a special character. It is really basic science, but on the other hand it shows how basic science can contribute to improved medical treatments and to business. It illustrates the special charter of this meeting."

He is not in favour of research that lacks some goal however. "Blue skies research – I don't like this term at all, you are doing science without a goal." You have a goal to develop improved therapies but also to see other benefits."This means jobs. That is a major goal here, to explain the importance of supporting basic science even though it might seem blue skies. From that definitely emerges jobs and therapies to disease."

O'Neill points to the more than 500 international scientists likely to take part in the meeting as evidence of Ireland's international standing in research. "More wanted to go on to the programme than can fit. They all know this is happening and are very enthusiastic," he says. "They know we are very good at immunology. We have a niche within the world of innate immunity. We are seen as one of the world centres in that."

> "He [Wallach] then suggested we hold a joint conference. What began as a chat over a glass of wine turned into this huge thing

It becomes a matter of pride for the scientists working in the Trinity institute. "The level of excitement; it is like Christmas coming for us in here."

The conference which started yesterday evening will be opened by the first of the five Nobel laureates, James Watson. The very full programme comes to an end on Tuesday evening. "We are asking people to to give their best stories," O'Neill says.

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- President of Ireland Young Researcher Award (PIYRA) aims to attract to Ireland exceptional early stage researchers.
- ERC Development Programme supports ERC applicants to resubmit to the ERC through an Irish Higher Education Institution.
- SFI Partnership Scheme aims to build strategic collaborations with key partners such as industry, funding agencies, charities, philanthropic organisations, etc. with the goal of co-funding outstanding research opportunities.
- SFI Conference & Workshops Programme supports the hosting of scientific meetings and conferences in Ireland.
- US-Ireland Research and Development Partnership supports research collaborations across the three jurisdictions, United States of America, Ireland and Northern Ireland.

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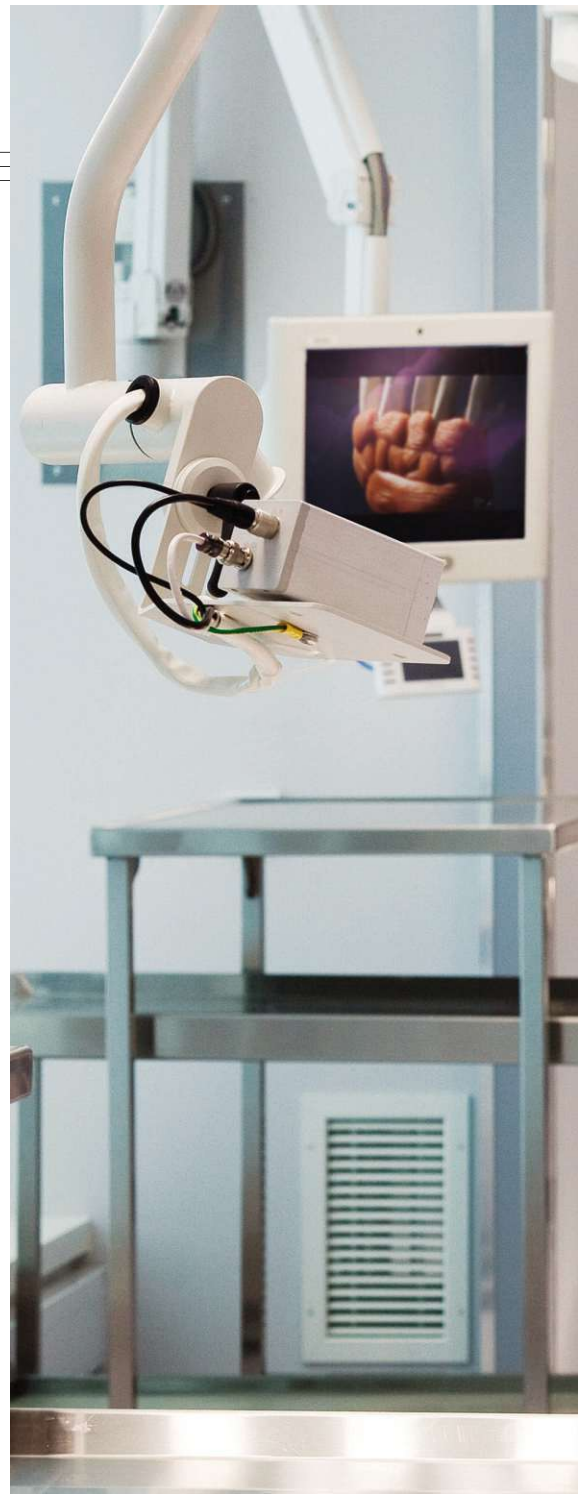
Driving discovery

The Trinity Biomedical Sciences Institute opened its doors on Pearse Street three years ago. **Claire O'Connell** reports on its history, scope and progress.



In science, working together works. That's the rationale behind the Trinity Biomedical Sciences Institute (TBSI), which opened its doors three years ago to accomodate researchers from a number disciplines so they could work cheek-by-jowl and learn from each other.

"We used to be in different buildings around Trinity, but an audit of biomedical research here said there was justification in bringing us all together in a purpose-built facility," recalls Prof Luke O'Neill, academic director of the TBSI and professor of biochemistry. "That started the ball rolling and by 2011 we had a new building on Pearse Street and groups from various disciplines started to move in."

The co-location of scientists working on vastly different questions but circulating together in the building was a key element to help drive new discoveries and ways of thinking, explains O'Neill.

"If you are trying to make a discovery you can't be restricted by your own biases and expertise, otherwise you may not make progress," he says.

"So you need to be open-minded and go where the action is – someone else might have techniques or approaches you don't have and if you go and talk to them and you each learn the other's language in science you might be the first to come up with new ideas."

Experiment yields results

The experiment of bringing scientists with different backgrounds in closer contact at the TBSI has paid off, according to O'Neill.

He points out that researchers at the institute have had more than 240 major publications to date, and between 2012 and 2013, TBSI researchers from different schools published 57 studies together.

The TBSI is meanwhile actively engaged in the commercial side of translating research, he notes – the institute is working with 76 companies and three companies have a presence in the building: Opsona Therapeutics, which has raised more than €65 million in funding and is modulating the immune system in kidney transplantation and other conditions; Trimod Therapeutics, which is exploring immunotherapy in cancer and Trino Therapeutics, which works in the area of inflammatory bowel disease.

Outreach is also high on the agenda. The institute hosts conferences, seminars and school visits, and O'Neill has a regular slot with Pat Kenny on Newstalk. In addition, the TBSI has a €1.8 million grant from the Wellcome Trust in association with Science Gallery Dublin to stage several public exhibitions.

The first, *Fat – It's Delicious* has just been rendered at the gallery, where members of the public could volunteer to take part in experiments, and the *Blood* exhibition is set to get pumping later this year.

"We have achieved a huge amount at TBSI within a few years and we are hoping for more of this, this is just the beginning," says O'Neill.

> "It suggests the same genetically determined diseases processes may manifest as psychiatric or neurodegenerative disease

Answering burning questions

The range of research covered by the 65 investigators and more than 500 researchers at the TBSI ranges from analysing molecules to exploring how parts of the body work.

O'Neill himself is a pioneering researcher in immunology – this month Thomson-Reuters put him in the top 1 per cent of researchers globally, in the *2014 World's Most Influential Scientific Minds* report.

O'Neill looks at how the body's frontline of defence works. Of particular interest is inflammation: externally we see its effects when the area around a cut becomes red and swollen.

Internally in the body inflammation is also a necessary part of our defences against injury and infection, but if it gets out of balance it can lead to life-threatening conditions such as sepsis or rejecting organs after transplant, or more slow-burning chronic conditions such as arthritis, heart disease and even cancer.

"We are trying to work out the nuts-and-bolts of the inflammatory process," says O'Neill, who recently published a paper in *Nature* about how cells

switch their fuel-burning mode during inflammation. "This change in fuel, this metabolic shift, is like putting the foot on the accelerator and revving the engine. But if you keep revving for too long it can cause damage, so we are finding ways to dampen it down."

From molecules to knees

Elsewhere in the TBSI building, Prof Martin Caffrey is studying the shapes of molecules called receptors. They span the thin fatty membrane that envelops each of the cells in our body, and they are of interest to medicine because they can detect factors outside the cell and trigger mechanisms to "tell" the cell how to respond.

> "If you are trying to make a discovery you can't be restricted by your own biases and expertise otherwise you may not make progress

Caffrey has developed a high-throughput method to prepare these complex molecules so that their structure can be worked out, leading to insights into how our bodies respond to stress and disease and opening more possibilities to design medicines that target them.

Another TBSI investigator, Prof Lorraine O'Driscoll, is examining how cancer cells respond to drugs and she is finding signals in the blood that could help to predict how a cancer is likely to behave.

Ultimately her work stands to help personalise treatments for patients so that they get the medicine that is right for their individual cancer.

And Dr Daniel Kelly is looking to "build" a biological knee or hip replacement using a patient's own stem cells. Stem cells from fat could be used to grow cartilage for small repairs and in the long-term he wants to use such stem cells to build an entire replacement joint in the lab.

Breaking boundaries

By working with researchers from other disciplines, TBSI investigator Prof Orla Hardiman is making discoveries about the brain. One of her most recent findings is a link between motor neurone disease, genetics and an increased risk of psychiatric conditions.

"What we are finding suggests the intriguing possibility that the same genetically determined diseases processes may manifest as neurodegenerative or psychiatric disease," says Hardiman, who is professor of neurology at Trinity and a consultant neurologist.

"It's an exciting finding and we have already started to build international consortia to study it."

For Hardiman, the TBSI provides an environment that brings her closer to collaborators and encourages creativity across disciplines.

"TBSI has a continuous flow of excellent keynote speakers, seminars and conferences that are stimulating and thought-provoking and that allow all sorts of outside-the-box thinking in a wide range of scientific domains."

Areas of interest: there are some 500 researchers at the TBSI working on everything from analysing molecules to 'building' biological replacement joints. PHOTOGRAPHER: DONAL MURPHY

Exploring a body of research

Scientists at TBSI conference will present their findings about the identity and functioning of biomolecules, writes **Prof David Wallach**

At the end of a scientific meeting some years ago, a heated discussion with my friend Luke O'Neill from the Trinity Biomedical Sciences Institute (TBSI) turned in to a friendly exchange on the approach to scientific research in our countries. We were struck by the similarities.

Both Ireland and Israel, despite limitations in size and resources, aspire to be at the frontline of research. But we also realised that most of our colleagues knew little about the research in each other's country, and we decided to do something about that. This supplement in *The Irish Times* concerns the first outcome of this plan, namely the conference from July 27th to 29th.

It introduces the subject matter of the conference, where leading scientists will present their findings about the identity and functioning of biomolecules, the nuts and bolts that comprise the body.This is a subject of huge importance: understanding the body's mechanisms of action is a prerequisite to understanding what goes wrong in pathological situations, providing us in turn with keys to treatment. Identifying a molecule whose function goes awry allows us to develop therapeutic drugs to counteract the aberration.

The conference will be attended by scientists from TBSI and Trinity College Dublin, and from the Weizmann Institute and several Israeli universities. It will start with a ceremonial signature on an agreement between the two institutes on funding for student exchanges and collaborative research. It will end with a session on the exploitation of basic science for drug development – a goal to which such ongoing collaboration can be expected to make a worthy contribution.

Prof David Wallach holds the Joseph and Bessie Feinberg Chair at the department of biological chemistry at the Weizmann Institute of Science

3 centres one for cancer drug discovery, one for immunology and one for medical device technologies

7 papers published in the prestigious group of *Nature* journals

Research by numbers Trinity Biomedical Sciences Institute

Trinity Biomedical Sciences Institute, or TBSI, was officially opened in 2011 on Pearse Street in Dublin, as a hub for outstanding scientific research. So what are its vital statistics? As of May 2014:

520 researchers work with TBSI in total

240 More than 240 publications in high-ranking journals

119 non-exchequer-funded jobs created in TBSI (since 2012)

76 companies engaged with TBSI researchers

10 million euro: the value of equipment at present in TBSI

7 scientific papers in the highly regarded journal Science

3 patents granted, including one on aspirin "prodrugs", or compounds that produce aspirin after they have been absorbed through the intestine

3 companies are based in TBSI, including Opsona Therapeutics, which has raised more than €60m to date in investment – €35 m in 2013 alone

Vital investigations Securing our grasp on biology

Trinity Biomedical Sciences Institute brings together 65 principal investigators who work in biomedicine. Their work has improved our understanding of:

- ✔ **the molecular switches on cells that switch on the immune system during infection or auto-immune diseases such as rheumatoid arthritis**
- ✔ **how our cells "sense" the presence of a virus**
- ✔ **the triggers that help set off fight-or-flight reactions when we are under threat**
- ✔ **how the immune system burns energy when fighting infection**
- ✔ **the genetics of motor neurone disease in Irish populations**
- ✔ **how tweaking the immune system may be able to make cancer treatments more effective**
- ✔ **genes involved in the skin condition atopic dermatitis, or eczema**
- ✔ **how the immune systems of animals such as poultry and cattle fight infection, opening the way for new vaccines and treatments**
- ✔ **how to assemble tiny chemical "nanosensors" to pick up important signals in the body**

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Basic science, big results

The Weizmann Institute of Science's research has had a huge international impact, writes **Peter McGuire**

It may be the most interesting and unique science research centre in the world. "There are very few places like this anywhere," says Yehiam Prior, professor of chemistry at Israel's Weizmann Institute of Science.

"We are a research-focused institution, our academics are free to research whatever we want and we are reasonably funded. Curiosity drives our decisions. Because we have no undergraduate students, we hire staff based on merit, not on filling a need for a teacher in a particular subject."

The institute was founded in 1949, and its first president, Dr Chaim Weizmann, led just a dozen staff; there are now about 2,700 people working there. Its influence can be felt in every part of Israeli society, including security, education and the economy. The Weizmann Institute produces about a quarter of all Israel's science PhDs.

The institute has research expertise in physics, chemistry, biology, biochemistry, maths and computer science, with additional research programmes in alternative energy sources, interplanetary science, robotics and more.

Basic research guides all their work, with their scientists driven by a curiosity to understand scientific principles and how nature works.

"We ask basic questions which do not have to have a clear commercial application," says Prof David Wallach who holds the Joseph and Bessie Feinberg chair at the Weizmann Institutes's biological chemistry department.

"This is because we cannot, for instance, find remedies for the diseases that we now cope with – including autoimmune problems, cancer, and circulation and heart disease – without understanding the mechanisms behind them."

It is no exaggeration to say that the institute has played a key role in the development of this young state. After one of the world's earliest electronic computers was built at the institute, the foundation for Israel's thriving software industry was laid.

The institute was the first to carry out cancer research and the first to build particle accelerators. Today, advanced vaccinations, nanotechnologies and drug research, particularly in the areas of multiple sclerosis and cancer, are among the many innovations on the horizon.

Almost half of the research conducted at the institute is focused on life sciences, and half of this research in turn is focused on cancer, making it one of the world's leading centres for cancer research.

Despite the focus on basic research, much of the work carried out at the Weizmann Institute leads to inventions with clear commercial possibilities.

In 1959, the Yeda Research and Development Company was established to identify, develop and license technologies arising from Weizmann Institute inventions. This has grown significantly; since 1959 it has registered about 1,400 families of patents. In 2011 alone, 163 agreements were signed, including 33 licensing and option agreements and 11 agreements with the EU.

Total sales of the products and technologies that grew from research conducted at the institute exceeded €15 billion over the past year."This has been one of the changes at Weizmann" says Prior. "It has always been an institute of fundamental research, but we are now much more active in utilisation of our intellectual property rights. The income is now quite high by global standards, not because we are encouraged or instructed to do applied research, but because the time-lag between basic research and inventions that emerge from that research has shrunk significantly. Copaxone, which is now used in the treatment of multiple sclerosis, is a good example of where Weizmann's researchers followed their nose and did some very good biology, which led to a drug that has changed millions of lives for the better."

Some of the more recent research carried out at the institute has led to deals with Adobe Systems for a product that reduces the size of still images or videos while maintaining the same level of detail; with Australian firm NewCO_2Fuels for a solar technology that turns the burning of coal into an environmentally friendly process; and with US-based Intelligent Imaging Innovations for the development of a new type of microscope.

The institute has always placed a strong emphasis on multidisciplinary research, with the campus serving as a meeting place for scientists from different areas. Each year, about 500 scientists from dozens of countries visit the institute or come to work on its campus. "We've organised a number of joint conferences across the world, including with the Pasteur Institute in Paris, McGill University in Montreal, and of course Trinity College Dublin," says Wallach. "We also have students and researchers from across the world, including Korea, China, Palestine, Russia and Ethiopia. Building relationships between researchers from across the world and contributing to the fraternity of nations is an important aspect of what we do."

> "The institute has always placed a strong emphasis on multidisciplinary research with the campus serving as a meeting place for scientists

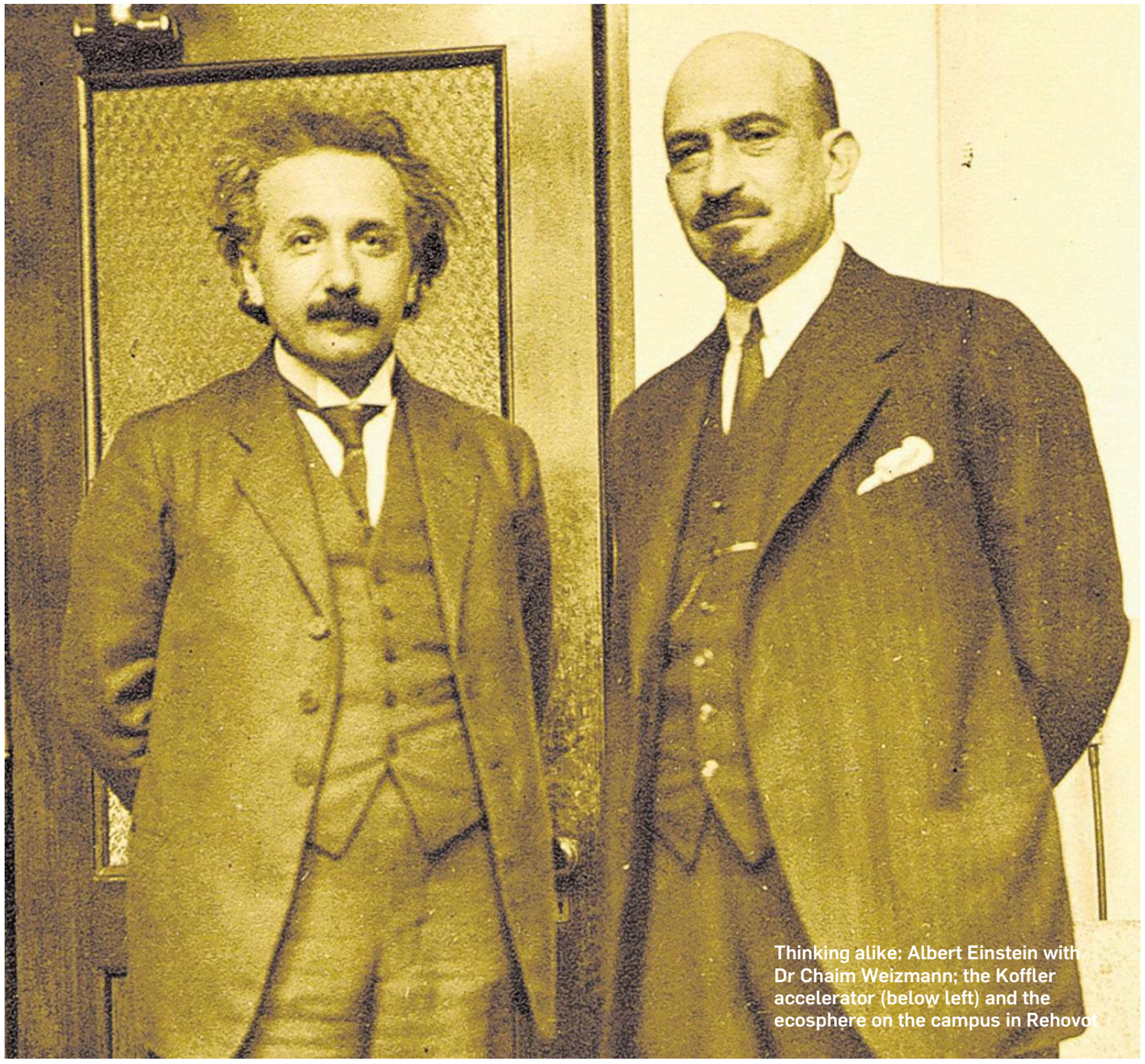
But the institute does much more than research. In 1958, the Feinberg Graduate School became its university arm, awarding MSc and PhD degrees in chemistry, life sciences, mathematics and computer science, physics, and science teaching. More than 1,000 students are enrolled, with English as the language of instruction.

Research students are trained for senior posts in academia, scientific and medical research, industry and governmental bodies. In addition, two summer science programmes offer 10- to 16-week placements for international undergraduate students.

The Davidson Institute, Weizmann's educational outreach arm, which was founded in 1999 to bridge the gap between the general public and science, to influence the education system, and to promote scientific thinking and understanding, has been a resounding success. It hosts public talks, informal meetings with scientists, exhibits, events, summer schools and workshops.

Davidson also provides professional development courses for maths and science teachers, and runs an innovative programme aimed at engaging disadvantaged young people in science.Prior has little doubt about the positive impact the Weizmann Institute has had.

"It is a wonderful example of something great that Israel has given to the world," he says. "Our graduates and inventions and ideas have made a significant contribution, and it has been such a pleasure for me to be here."



Thinking alike: Albert Einstein with Dr Chaim Weizmann; the Koffler accelerator (below left) and the ecosphere on the campus in Rehovot

Examining nature
Discoveries in Rehovot

❒ The structure and function of the ribosome: In 2009, Prof Ada Yonath was awarded the Nobel Prize in Chemistry for discovering the secrets of the cell's protein factory and revealing its means of action. Her research is being used to speed up the development of more efficient antibiotics.

❒ Medical marvels: A number of drugs developed at the institute have transformed the lives of millions, including Copaxone and Rebif, which are used both used for the treatment of multiple sclerosis, and a vaccination for hepatitis B. The institute also created a method for bone marrow transplants from mismatched donors, as well a non-invasive method for distinguishing between malignant and benign tumours using magnetic resonance imaging.

❒ Amniocentesis: Familiar to millions of parents worldwide, this prenatal fetal diagnostic test was developed at Weizmann.

❒ Transforming agriculture: Scientists at the institute have developed improved crop varieties, including early-ripening melons, protein-rich and high-yield wheat, and disease-resistant cucumbers. They have also pioneered a method for growing hybrid seeds that prevents the transmission of disease from one generation to the next and helps protect edible plants from pests.

❒ Affinity chromatography: A vital tool used for purifying biological materials in the biotechnology industry.

❒ Living polymerisation: One of the most important techniques of the modern plastics industry.

At a glance The Weizmann Institute

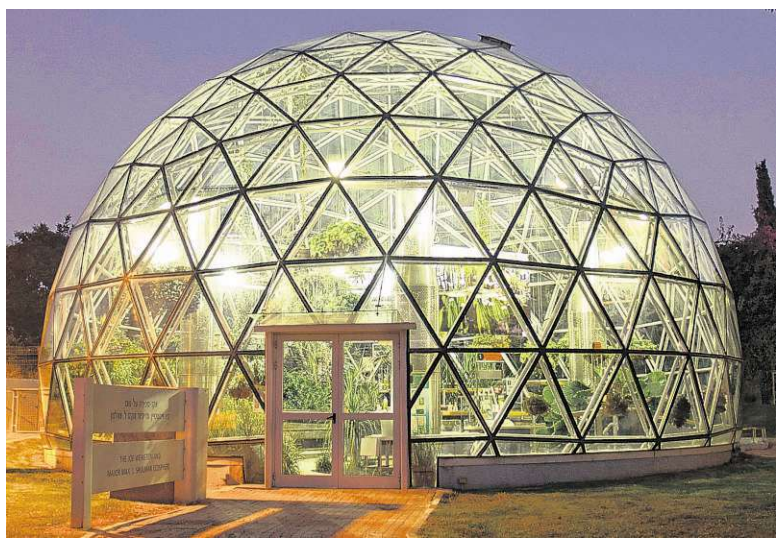
❒ About 1,200 research projects are taking place in the institute at any given time, across 250 research groups.

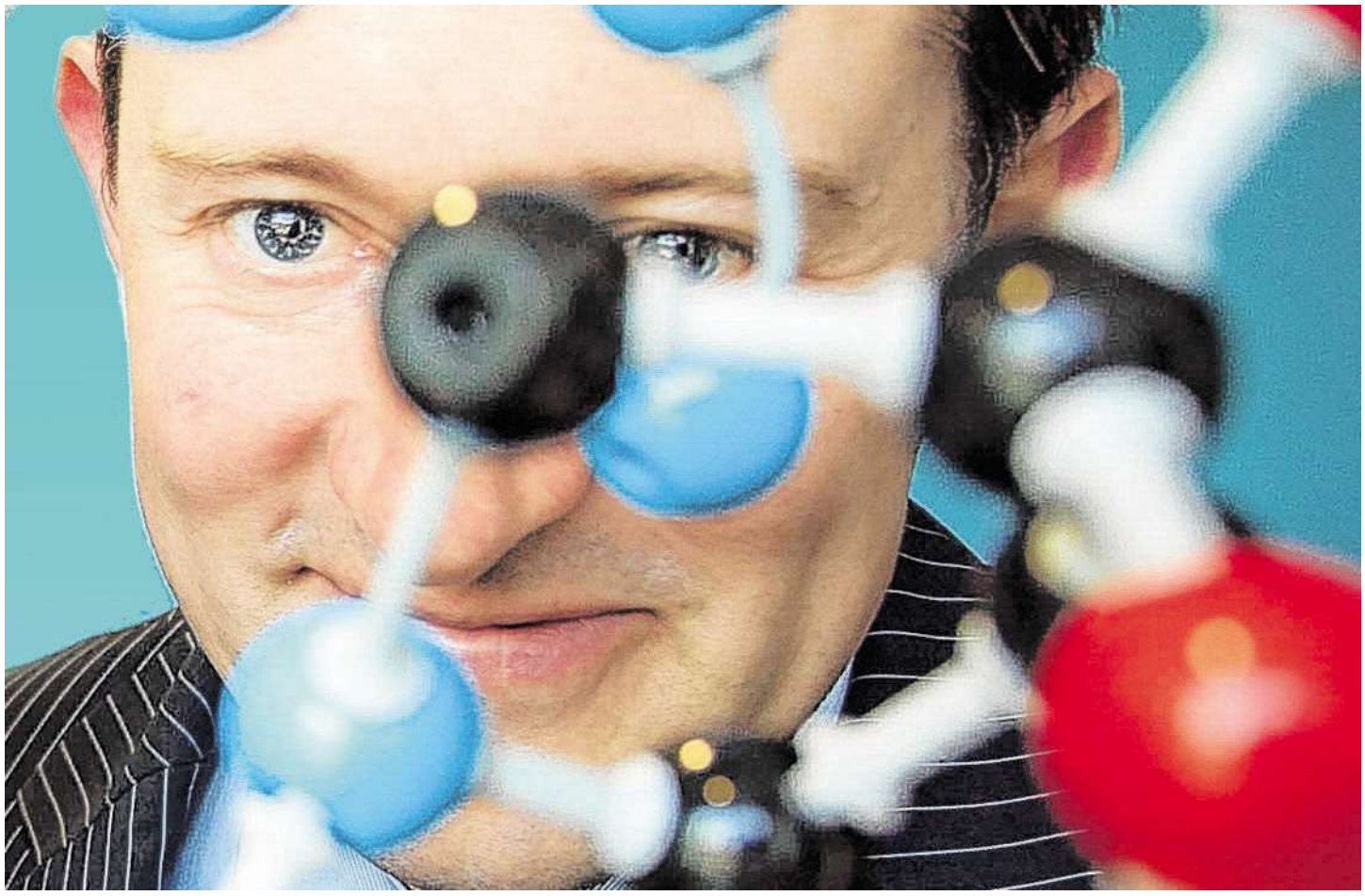
❒ The institute houses 1,076 research students and 380 postdoctoral fellows across the faculties of mathematics and computer science, physics, chemistry, biochemistry and biology. These are divided into 18 academic departments.

❒ The institute contains 50 multidisciplinary research institutes and centres, which enable the development of joint projects across diverse fields, including nanotechnology, renewable energy, experimental physics, cancer research, genetics and more.

❒ The campus covers 280 acres, including more than 100 buildings and 94 acres of lawns, shrubs and orchards.

❒ The institute's annual budget is more than one billion shekels, or about €214 million.





Pioneering teamwork

The symposium will catalyse a strategic link between TBSI and the Weizmann Institute, writes former Minister of State for Jobs, Enterprise and Innovation, **Séan Sherlock**

I very much welcome the upcoming joint symposium between the Trinity Biomedical Sciences Institute (TBSI) in Trinity College Dublin and the renowned Weizmann Institute of Science in Israel, which will lead to increased cooperation between the two institutes.

No fewer than five Nobel Laureates will deliver keynote addresses on the subject of medical research, in particular on cutting-edge progress in the fight against inflammatory diseases and cancer, at this three-day symposium. These are extremely important and significant societal challenges for the world's population.

Nobel Laureates such as geneticist James Watson, biologist Aaron Ciechanover, immunologist Bruce Beutler, chemist Ada Yonath, biologist Jules Hoffmann, as well as the illustrious immunologist Marc Feldmann will all attend the discussions.

The symposium started on the evening of July 27th, with the official signing of a memorandum of understanding outlining the planned co-operation between the TBSI and the Weizmann Institute. The partnership will include a cooperative project of joint symposia and an exchange of students between the two institutes.

The TBSI is endeavouring to promote close, strategic links with global centres of excellence and this highly promising initiative can be seen as a pioneering collaboration between two of the world's leading research institutes in the field of biomedicine. The Weizmann is a hugely successful research institute on a world scale which can, in effect, act as a model for the TBSI.

It is hoped that this is just the beginning of a fruitful relationship and that there will be further collaboration between the two institutes. The Weizmann Institute carries out cutting edge research in immunology and cancer, with excellent facilities and approaches.They also have a very impressive record in technology transfer, which Trinity College students will be exposed to.

Here, the TBSI is an environment where innovative and interdisciplinary approaches are leading to scientific discoveries of biomedical importance in infectious and inflammatory diseases, including cancer, ultimately giving rise to better patient care.

It was established with the help of the Higher Education Authority and the Programme for Research in Third-Level Institutions in 2011 and receives ongoing funding from Science Foundation Ireland among others, enabling it to excel in a range of disciplines related to biomedical research.

The activities of the TBSI are very much in line with the National Research Prioritisation Exercise, of which five of the 14 priority areas are explicitly related to the health domain, including diagnostics and therapeutics, synthesis, formulation, processing and drug delivery. In addition, basic biomedical science is one of the six areas of platform science and technology which are underpinning research prioritisation.

> “It is hoped that this is just the beginning of a fruitful relationship and that there will be further collaboration between the two institutes

Seán Sherlock at the launch of the Science-2-Business programme.
PHOTOGRAPH: SHANE O NEILL/FENNELLS

I would like to acknowledge the contribution of Professor Luke O'Neill, academic director of the TBSI and his counterpart, Prof David Wallach of the Weizmann Institute , in organising this progressive initiative.

Finally, I would like to wish the TBSI continued good fortune with their very worthy endeavours in the important area of biomedical research, and success with this much anticipated symposium.

Seán Sherlock TD is now Minister of State at the Department of Foreign Affairs

ADVERTISING FEATURE

ROCHE IN IRELAND

Roche is a leading supplier of diagnostic systems to hospitals and medicines for cancer and viral diseases. Roche also is a leading supplier to Life Science research laboratories. The Group has three operations in Ireland, including a manufacturing site in Clarecastle. Roche employs approximately 340 people in Ireland. Roche Diagnostics in Ireland is part of Roche Diagnostics Limited based in Burgess Hill, West Sussex, UK. In addition many Roche Diabetes Care blood glucose testing devices are manufactured under contract in Ireland, for example by Sanmina Sci in Co. Cork.

Roche's Irish Commitment

Roche believes that its involvement with the communities in which it operates contributes to its success. In Ireland Roche works closely with the local community in a variety of ways:

Community

Roche in Ireland works closely with the local community through a Community Liaison Group, which comprises company and local representatives. This group updates people living in the locality with anything happening on-site and is the forum for discussing issues or concerns.

Supporting Science and Education

Roche supports the advancement of science and education In Ireland in a variety of ways, such as hiring student placements, scholarships which support employees' children through tertiary education and job shadowing for teachers. Some examples of these initiatives are:

- The Junior Achievement Programme which creates a link between the classroom and the world of work. Roche employees are encouraged to volunteer in the programme by teaching in primary and secondary schools, encouraging students to continue in their education and teaching them the skills they need to succeed in a changing world.

- The Roche Research Awards, which coordinates an annual Research Award scheme within each of the major academic centres in Ireland, recognising and awarding excellence in Life Science research. This highly successful initiative has highlighted Roche Diagnostics' investment into Irish research and has consolidated key strategic relationships within a volatile and financially-pressurised academic environment.

- Collaboration in a recent funding initiative between the Department of Jobs, Enterprise and Innovation and the Pharmaceutical Industry which saw the award of €40million funding to the University of Limerick's Synthesis and Solid State Pharmaceutical Centre, which will create 90 research jobs over the next six years.

Charities

Locally, Roche undertakes a number of fundraising activities throughout the year in order to raise money for various causes. The Roche Children's Walk takes place annually and all monies raised by employees are matched by the company. The proceeds go towards supporting vulnerable children.

Roche has given generous contributions to local charities such as the Burren Chernobyl Project, the Laura Lynn Foundations and St. Mary's National School in Tallaght as well as making donations to the Irish Cancer Society.

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and neuroscience. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostics that enable tangible improvements in the health, quality of life and survival of patients. Founded in 1896, Roche has been making important contributions to global health for more than a century. Twenty-four medicines developed by Roche are included in the WHO Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and chemotherapy.

In 2013 the Roche Group employed over 85,000 people worldwide, invested 8.7 billion Swiss francs in R&D and posted sales of 46.8 billion Swiss francs. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan.

For more information, please visit www.roche.com.

Making science pay

Technology transfer, the monetisation of research in the form of patents or spin-out companies, is crucial for continuous innovation, writes **Fiona Reddan**

It is not enough for today's universities and research institutes to make a new discovery or scientific advance. Transferring those research discoveries to industry must also be high on the agenda, to ensure that any discovery can be developed and commercialised to benefit both the public, and the taxpayer, through additional revenues and job creation.

It is this ability to convert its research findings and academic knowledge into practical applications – for the improvement of health and standards of living – through cooperation with commercial entities, that has seen Israel's Weizmann Institute flourish.

Since the inception of its technology transfer arm, the Yeda Research and Development Company in 1959, the Weizmann Institute has registered 1,833 families of patents and is ranked in the top 10 tech transfer companies worldwide in terms of revenues. It has discovered numerous groundbreaking medical and technological applications including the development of amniocentesis – a prenatal diagnostic test of the amniotic fluid that surrounds foetuses – and sophisticated laser systems for high-precision diamond cutting.

And now, thanks to a collaboration with the Trinity Biomedical Sciences Institute (TBSI), experts from the Weizmann Institute are coming to Dublin to present at a symposium to be held in conjunction with the TBSI about research into cancer, immunity and inflammation.

But what is the secret to its success?

Part of the Weizmann Institute's success in commercialising its research is that it has "been doing it for a very long time", says Prof Mordechai Sheves, vice president for technology transfer with the institute.

> "The Weizmann Institute takes a fundamental approach to its research and is prepared to invest the money at the expensive early stage

Collaboration is also "very important" in successfully commercialising research says Sheves. "Collaborations– with good institutes like Trinity – can help a lot."

But it's also because the Weizmann Institute takes a fundamental approach to its research and is prepared to invest the money at the expensive early stage.

"Tech transfer is based on good science. Everything starts from good basic science," says Sheves. "We don't aim to develop technologies. We want to understand nature and are driven by curiosity."

It's a perspective that Prof Luke O'Neill, academic director of the TBSI, agrees with.

"We don't set it up [tech transfers] as a way to make money," says O'Neill. "What we're trying to do is make discoveries that would help in the treatment of inflammatory diseases or rheumatoid arthritis. What we're trying to do is make discoveries".

Such an approach is not cheap however.

"Basic science is expensive. You have to take risks, otherwise you won't discover important things," says Sheves.

It can also take a long time for projects to come to fruition. Opsona Therapeutics, for

Spinning out: Prof Mordechai Sheves (right) of the Weizmann Institute believes technology transfer is based on good, basic science. PHOTOGRAPH: ALLAN H SHOEMAKE/GETTY

example, a clinical stage biopharmaceutical company that was spun-out of Trinity, has received funding of some €50 million since 2004, one of the highest levels received by any Irish biotech company. It is still waiting to make a return however.

Fundamental research is "high risk, very expensive, and can take 15-20 years to realise commercial potential," says O'Neill. "It takes a billion dollars for a drug company to develop a drug . . . the most difficult thing humans can do is to discover a new drug," he adds.

So should Ireland seek to emulate the Weizmann Institute's approach and put money into fundamental research or opt to support innovations that may be closer to market?

"Clearly you should try to fund both if you have the money," says O'Neill, noting that many countries tend to fund more applied research and there is a lot of competition in this sphere.

"You need to be pragmatic but if you neglect fundamental, you won't give rise to economic advances either," he adds.

Mark Ferguson, director general of Science Foundation Ireland and chief scientific adviser to the Government, agrees that Ireland needs a "portfolio approach" to its research agenda.

"Some fundamental research won't be of any use. But some of it will be disruptive - and that's where we need to be, we need to have it," he says.

But if basic science is expensive, tech transfers can help to ease the funding requirements, and according to research institutes, it's a way to "give back" to the governments that have helped fund them.

"We'd like to help the country economically," says O'Neill, noting that this can take the shape of encouraging spin-outs to form, undertaking licenses, or doing contract work for drug companies.

Indeed, the TBSI has raised €36m in research funding, creating 119 jobs since 2012, while it has also spun-out three companies: Opsona, Trino and TriMod.

"Clearly, if we are funding scientific research in Ireland from taxpayers' money, and some of these give rise to inventions that are commercially viable, then the taxpayer will want a return and that's job creation – and also revenues if it's a particularly useful invention," says Ferguson.

And, while Sheves notes that "the most important thing is that society enjoys Weizmann," he concedes that economic goals are important too.

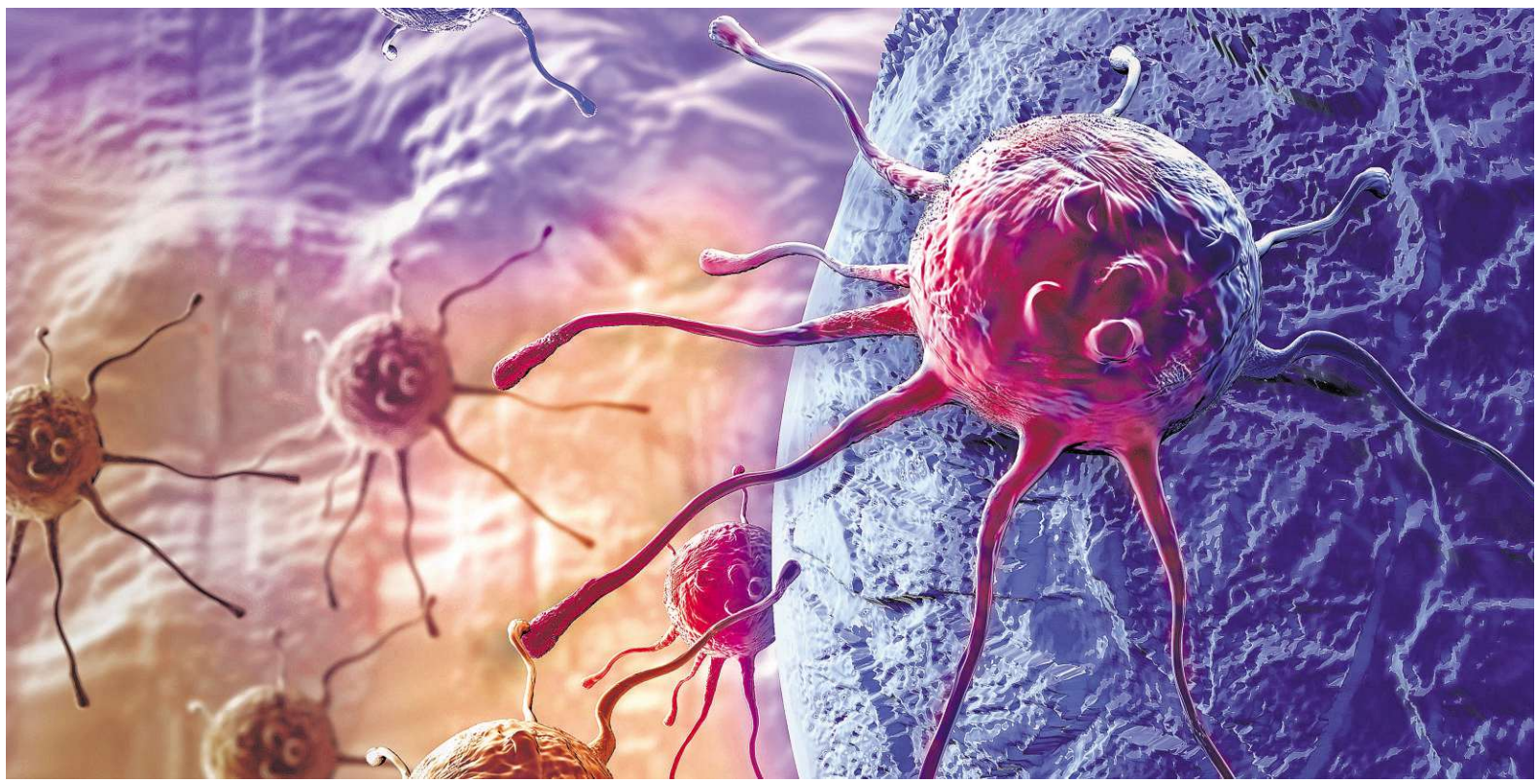
"Research has become more and more expensive, and the economic benefits from tech transfer allow us to do good basic science," he says.

But how do you choose which areas to fund?

For O'Neill, it comes down to excellence.

"As long as you fund excellence you will get a good return," he says.

This is a view echoed by Ferguson: "Small countries like Ireland and Israel are not scaled down versions of large countries. We can't afford to do everything – we wouldn't have enough money. So we have to choose areas where we can be internationally competitive".



Cancer attacked on all fronts

A collective of expertise, including physicists and mathematicians, is looking at the molecular triggers behind the most complex and destructive of diseases, writes **Dick Ahlstrom**

Cancer research is undergoing a revolution, with many sciences joining together to tackle this huge health issue. It brings together biologists with biochemists, physicists, mathematicians, chemists, drug designers, clinicians and other disciplines to unravel this most complex of diseases.

Cancer is a particular target for the Weizmann Institute and Trinity Biomedical Sciences Institute (TBSI) and both centres – who began a three-day conference on July 27th – are making great strides using advanced technologies.

"It isn't so much focused on particular cancers as in the past, it is more focused on molecular discovery," says Prof Gavin Davey, head of the school of biochemistry and immunology at Trinity College Dublin. "It is about discovering new biomolecules that control cancer cells of any type."

"We are undergoing a real revolution, more than a revolution, where people are joining together and in doing so bringing in a lot of technology you could not handle without mathematical tools," says Prof Varda Rotter, a recent head of the department of cancer research at the Weizmann Institute and a principal investigator there. "Instead of looking at one variant of cancer you can look at an entire transcriptome [what the genes are producing] and the complete genome [the entire genetic blueprint]."

The combination of expertise has opened up exciting new avenues of research when looking for the underlying causes of cancer. The body's powerful immune system is also being brought into play against cancers. "We do a lot in designing antibodies and biotherapeutics, typically antibodies artificially made that target cancer cells," says Davey who is director of the cancer drug discovery research group within Trinity's institute.

"They bind to the cancer cell and signal for the immune system to attack using natural killer cells. The immune cells are very aggressive at killing cancer cells," he says.

"People are also looking at how the immune system controls cancer cell development. This is a big area that has exploded in recent years – immune system-cancer interactions. We also spend a lot of time developing biotherapeutics. That is really revolutionising cancer treatment but there is a lot more to be done."

The application of molecular biology – discovering the biochemical signals that drive cancer – has made a huge impact, but this is now linking up with what is known about the immune system.

"I was trained as an immunologist and did a PhD in it 35 years ago, but then all the immunologists who wanted to tackle cancer thought it would be good to move to molecular biology. Now 35 years later people are back applying immunology to the disease," says Rotter.

"It is very important that science marches with time. In these years of molecular biology we all started with very simple systems looking at one gene, one protein, two proteins, but due to the great developments in molecular biology you can take a global look into the cell, a system look into the cell," she says.

Data can be collected but there is too much for an individual to unravel. Mathematicians can develop models that crunch the numbers and reveal the hidden signature of a disease or a key gene. "We are recruiting young people coming from systems biology approaches and that is what is making the difference," says Rotter. "This melding of different fields is helping to make the Weizmann Institute one of the leading powers in cancer research."

The TBSI has taken a similar approach with many different scientific disciplines being brought to bear on cancer research, Davey explains. The biochemists pinpoint a gene and protein of interest and then the chemists take over, designing new drugs that can target the protein, either boosting its activity or blocking it depending on what it is doing in relation to the disease.

Cancer cells: the disease is a particular target for the Weizmann Institute and Trinity Biomedical Sciences Institute – both have made strides in the area.
ILLUSTRATION: THINKSTOCK

"People are developing vaccines against cancer, others are looking at the carbohydrate chemistry in cancer cells," he says. "The focus here is on discovering new molecules that drive cancer. We have brilliant immunologists, cell biologists, chemists, bringing them all together and working together to tackle cancer," he says. "It is all about fundamental discovery."

Trinity's institute has about 150 researchers working in 25 distinct research groups but it can be difficult now to separate who is working on cancer and who is working on immunology, suggests Rotter. "Cancer research is really being conducted on many different levels today and all of these can go under the title cancer even though those involved work in different departments."

It all comes down to maintaining "good contacts between complimentary experts", she believes.

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Preparing the patient

Prof **John Reynolds** on taking a personalised approach to patient care

A personalised approach to patient care and a fresh focus on preparing the patient for the rigours of cancer therapy are on the research agenda pursued by Prof John Reynolds , Trinity College professor of surgery, who specialises in surgical oncology of the oesophagus and stomach. It is highly translational, with the goal to improve treatments, he says.

His group conducts detailed molecular and immunological studies of a patient's fat tissue, liver and blood in patients going forward to surgery. "We are looking at the links between lifestyle and cancer risk in pathways associated with inflammation," he says.

They are also looking at whether they can predict how a patient will respond to a treatment by looking at biopsy tissue before going into oesophageal or stomach surgery. "This is moving towards personalised medicine, and novel trials using what we know from the translational science." Obesity is a major risk in oesophageal cancer but another important predisposing factor is chronic reflux, when stomach acid comes up from the stomach into the oesophagus. Some of these will have a pre-cancerous condition called Barrett's oesophagus, he says. They are looking for ways to predict which Barrett's patients can be left alone and which may need "a preemptive strike".

Another novel approach is to bring physiotherapists and dieticians together with the medical team to help a patient about to undergo difficult treatments. It involves "prehabilitation, getting the patient ready before treatment", and then following up during rehabilitation. "The more major the intervention the greater the logic in trying to prepare and optimise the patients."

– Dick Ahlstrom

Trojan horse is activated by beam of light

Prof **Thorri Gunnlaugsson** on fighting cancer with metals

Greek literature tells us how a Trojan horse helped win a war by carrying hidden attackers. A similar approach is being used by chemists at TBSI who are attacking cancer cells using concealed metals.

"We have been making organic compounds that are carrying metal complexes based on ruthenium," explains Prof Thorri Gunnlaugsson, professor of chemistry. "We have been able to show that it is taken up by cancer cells very rapidly."

The approach is very different from using chemotherapy where a toxic chemical is used to kill cancer cells. But these substances also damage healthy tissues and can make patients ill.

These chemical complexes based on ruthenium are different. They are not toxic when administered and taken up by the fast-growing cancer cells, the perfect Trojan horse. But they change character completely and attack the cancer when activated by a beam of light.

"They are not toxic but can become activated with visible light. It promotes an excited state and within this state they can do chemistry and become toxic in situ," he says. They can trigger the cancer cell to go into cell death in a controlled way.

Using ruthenium has a hidden benefit. "The good thing about these compounds is they are luminescent so we can watch their uptake into the cells without having to use other compounds to visualise them," Prof Gunnlaugsson says.

Working with colleague Prof Clive Williams, professor of chemistry and his team, he is looking at the possibility of using nanoparticles as a carrier for the ruthenium. "We can use them like a vehicle. And they could be magnetic so we could direct them to where they are wanted."

– Dick Ahlstrom

Trying out illegal drugs

Prof **Clive Williams,** looks at chemical signatures of home-made drugs

An analysis of illegal home-made drugs has resulted in a promising new treatment for cancer. The chemical compound induces death in cancer cells and holds promise as a treatment against adult leukaemia.

The work is a collaboration between Prof Clive Williams and Prof Mary Meegan in pharmaceutical chemistry, both at Trinity College Dublin. It got underway when Prof Meegan began searching for "chemical signatures" in illicit amphetamines as a way to identify the manufacturer, explains Prof Williams who is professor of chemical biology and dean of the faculty of engineering, maths and science. The "home-cooked" drugs are full of by-products and these can point to the maker. She assembled a library of novel compounds and the two scientists, who have collaborated for 40 years, decided to see if any were toxic to cancer cells.

"We screened all 240 of them and picked three compounds with slightly differing characteristics," he says. They were all nitorstyrenes and they recompounded them for use in tests using blood cancer cell lines and blood from patients with these cancers. We found they could kill cancer cells quite potently, causing apoptosis, the natural process of cell death. We are at the stage where we have made lots of compounds and gauged their activity, and are taking a few forward to see how effective they are at killing cancer cells such as chronic lymphocytic leukaemia in adults.

"We try the compounds depending on what our clinical colleagues suggest might be ones to try. Their problem is lots of cancers mutate very quickly so new compounds don't remain effective over time," he says. That is why it is valuable to identify new toxic agents that can be used in the battle against the disease.

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How to block growth

Prof **Yosef Yarden**on taking away the substances that promote tumour growth

One way to slow cancer is to take away the substances that promote its growth. This can halt the cancer in its tracks and leave the tumour more susceptible to chemotherapy and radiotherapy.

This is the approach being taken by Prof Yarden and his team of 20 who are developing ways of inhibiting the "epithelial growth factors" that are vital for tumour growth.

"They need these special factors," says. Yarden who is research group leader in cancer at Weizmann's department of biological regulation. "Without them the cancer cells can't proliferate and can't migrate from the primary tumour to metastasise.."

His team is delving into the complex biochemistry where such factors interact with the tumour. And they are using several methods to interfere with this interaction. He was amongst the first to develop antibodies as a way to achieve this.

Antibodies are a part of the immune system, but those developed by Prof Yarden are custom made to attach themselves to the surface of cancer cells, at the specific places – called receptors – where the growth factor would normally attach itself.This leaves no room for the growth factor. "If you can block them, then they effectively block those growth factors and the receptors," he says.

Denying the tumour essential growth factors does not in itself kill it off. "Usually the cancer is arrested, not cleared." But in this state they become more susceptible to chemotherapy and radiotherapy. His team is also assessing novel drugs arising from the research. "We are highlighting the basic science that is needed to develop some useful, effective drugs."

– Dick Ahlstrom

Finding cancer cells' hiding place

Prof **John O'Leary** on molecular activity between platelets and cancer cells

It is like a wolf in sheep's clothing when cancer cells from a primary tumour break off and start to colonise new sites. They cloak themselves in platelets circulating in the bloodstream and use this trick to elude treatment.

O'Leary and his research group, along with Dr Clair Gardiner, were among the first to discover this trick, which helps cancer cells that break off to circulate around the bloodstream.

It allows them to hide from attack by the body's immune system by masquerading as normal cells. It also helps protect the cancer cells from shear forces when moving through the blood stream, says O'Leary who is professor of pathology at Trinity and consultant pathologist at St James's and the Coombe hospitals,. "We are studying in detail the molecular activity between platelets and cancer cells," he says.

"Platelets also give a signal to the cancer cells telling them not to die by turning off apoptosis [natural cell death]." They also turn on genes needed for cell growth and building a blood supply.

> "We have looked at the effect of treating the platelets with aspirin and inhibitors and we can partly reverse the interaction

"We have looked at the effect of treating the platelets with aspirin and inhibitors and we can partly reverse the interaction." It interferes with the cancer cells' ability to invade new cells.

He has active research underway into stripping away the cancer cells' ability to hide and another line of inquiry trying to block the "pro-survival" signal sent to them from the platelets.He is also trying to help the innate immune system to remember what its proper job is and go back to killing off these aberrant cells.

He is doing this by looking back to what platelets do in the foetus during early development.

"Platelets are very important during pregnancy," he added.

Looking to convert the mutants

Prof **Varda Rotter** co-discovered the P53 tumour suppressor gene

One of the most important discoveries in the field of cancer research relates to the p53 tumour suppressor gene. When it is working properly it acts like a policeman, knocking out aberrant cells but when p53 itself is mutated then the outcome can be cancer.

The p53 gene was discovered by Prof Varda Rotter and her research colleague Prof Moshe Oren decades ago. It triggered research around the world that has deepened our knowledge of how cancer works."Cancer develops when genes or our genetic material is being damaged. Our bodies have developed all kinds of mechanisms which prevent cancer and that is mediated by tumour suppressors like p53," Prof Rotter, who is head of Molecular cell Biology at Weizmann, explains.

Research has shown what happens when the p53 good cop goes bad. "This is a mechanism found in 50 per cent of tumours but there are also tumours that have lost other guardians but p53 is a very common reason for cancer. So what to do about it. How can you reeducate the mutant to go back to being a good police man," she says.

The developing foetus may hold the answer. It has mechanisms that force a mutated p53 to revert back to a normal p53. It helps to ensure that mutated cells are destroyed and keeps the tumour suppressor activity working. She and Oren have labs studying this, "looking for methods to convert the mutant into a good one", she says.

Drug designer techniques called into play

Prof **Irit Sagi** on why scientists think outside the cell

Analytical and imaging tools originally developed to serve physics and chemistry research are being used at the Weizmann Institute to study complex biological processes. The goal is to visualise the entire microenvironment of a cell along with the matrix in which it sits.

"That is what is unique to our laboratory. By including analytical tools it gives us a lead in drug design," says Prof Sagi who is dean of the graduate school and department of biological regulation at Weizmann.

"The thing we are investigating is the remodelling of the cellular microenvironment. We go from biological principals to drug design," she says. "What we are doing is a multidisciplinary approach to studying the cell."

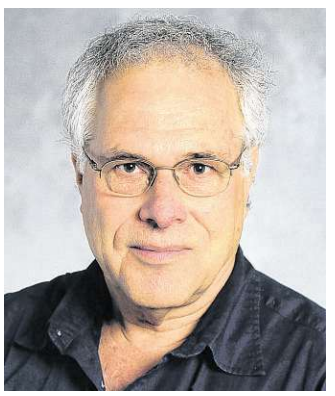
Defining small elements of cellular activity cannot provide a complete picture, for this you need to take a wider view. "People ask why as scientists we think outside the cell. It is because the cell is embedded in a whole matrix, it is not only a scaffold it is a reservoir used for signalling," Prof Sagi explains.

"Inflammation and cancer harness this extracellular enzymology in order to make tissue or progress the disease. All this enzymology can be blocked by molecular modulators and we use them to mimic normal inhibitors to block inflammation and cancer," she says.

"Once we find a main molecule we study it in fine detail using all kinds of physical tools, x-ray, infrared, and combine all this data in a mechanistic model. Then we use drug designer techniques like protein engineering."

– Dick Ahlstrom

Cells that fight cancer



Prof **Zelig Eshhar** on 'immune memory'

When the body is trying to fight off cancer, it can do with all the help it can get.

Prof Eshhar, professor of immunology emeritus, is involved in research that creates immune cells that have been shown in patients to attack the tumour and stop the disease.

"The research involves a redirection of T-cells that naturally fight viruses and transplanted tissues," says Prof Eshhar. They also attack mutated cells, but when cancer takes hold the T-cells no longer see cancer cells as the enemy, allowing them to grow and spread."In this case we have developed a way to redirect the T-cells to recognise the tumour again and the way we did it is with a chimeric antigen receptor," he says.

This involves taking T-cells from the patient and then engineering them, adding an antibody that automatically wants to attach itself to the cancer cells.

When these modified immune cells are reintroduced into the patient, the added antibody locks onto the cancer and the T-cells once again recognise the cancer as "enemy".

"When they reach the tumour they also propagate because that is what T-cells are geared to do," he says. This builds up the number of attackers and it also creates an "immune memory" against the cancer should it ever appear again, just like it does against a virus.

Trials conducted over the past three years in the US and UK in end stage patients with blood cancers showed it was successful in more than 30 per cent of cases, "not just halted it, but complete remission of end stage patients", he says.

Meet the speakers

Five Nobel laureates, including co-discoverer of the structure of DNA James Watson, are among the 24 speakers at the conference who will talk about basic science with the expectation of inspiring new advances, writes **John Holden**

So much research around the globe goes into the search for novel treatment and therapies for far-reaching diseases like cancer, autoimmune diseases and arthritis. However, without joined-up thinking, it is frequently the case that research being carried out in one lab – that could be of use in another – never reaches a wide enough audience. This can mean that potential new treatments, therapies and cures are not realised.

The Trintity Biomedical Science Institute (TBSI)/Weizmann Institute of Science conference is an attempt to bring like-minded people together in the hope that cross-collaboration will lead to important new discoveries.

The presence of five Nobel Laureates on the programme should provide ample inspiration for young scientists in attendance to push for novel research approaches.

"Professor Luke O'Neill and I are both studying in the field of bio-inflammation, which will be a major focus of the conference," explains Prof David Wallach of the Weizmann Institute.

"However, a number of related branches of biomedicine will also feature including research by both institutes into several diseases; such as rheumatoid arthritis, MS, motor neuron disease, inflammatory bowel disease, leukemia, major cancers, etc and how best to control or eradicate them in the future."

The event, which is largely down to Prof Luke O'Neill of the TBSI, has been in the pipeline for some time. "It will be fantastic," says O'Neill. "This will be the biggest conference ever in Trinity, with five Nobel laureates giving keynote speeches as well as a whole slew of other people; ten speakers from the Weizmann Institute and 14 from TBSI, with seven keynote speakers in all."

One of the keynote speakers is Bruce Beutler, the 2011 Nobel laureate in physiology and medicine. Beutler won the award for his work on how mammals "sense" infection. In fact, he shared the honours with one of the other keynote speakers, Jules Hoffmann, for their joint "discoveries concerning the activation of innate immunity" as the official website of the Nobel Prize.

Aaron Ciechanover, who won the 2004 Nobel Prize in chemistry, received his award for his work on ubiquitin; the substance cells use to breakdown and recycle proteins. Hence the title of his presentation in Dublin: The Ubiquitin Proteolytic System: From Discovery Through Basic Mechanisms, and on to Human Diseases and Drug Targeting."

The 2009 Nobel laureate in chemistry, Prof Ada Yonath, is based in the department of structural biology at the Weizmann Institute and will also be one of the keynote speakers. "I am currently studying protein biosynthesis according to the genetic code," she says. "In my field, one of the major issues currently of concern is antibiotics resistance.

"I will be discussing these areas as well as the burning medical problems concerning resistance to antibiotics, focusing on the species specific mechanisms for acquiring resistance."

Winner of the 1962 Noble Prize in physiology and medicine, James Watson (see panel), who, working with Francis Crick, first described the structure of DNA, is also sure to draw a large crowd.

Professors Luke O'Neill and David Wallach will also speak along with 14 other Irish scientists: Kingston Mills, Aisling Dunne, Cliona O'Farrelly, Gavin Davey, Seamus Martin, Martin Caffrey and Diarmuid O'Brien, among others.

Professor of experimental immunology at Trinity College, Kingston Mills will be speaking during the inflammation section. "A lot of my presentation will impinge on latest developments for treating autoimmune diseases such as multiple sclerosis, Chrone's disease, rheumatoid arthritis, etc," he says.

"Currently we know around 20 percent of the world's population will get an autoimmune disease and they are currently treated with various steroids. But more and more, sufferers are being treated with biological drugs, some of which are made in Dublin by Pfizer. The way forward for treating autoimmune diseases is finding inhibitors," he adds.

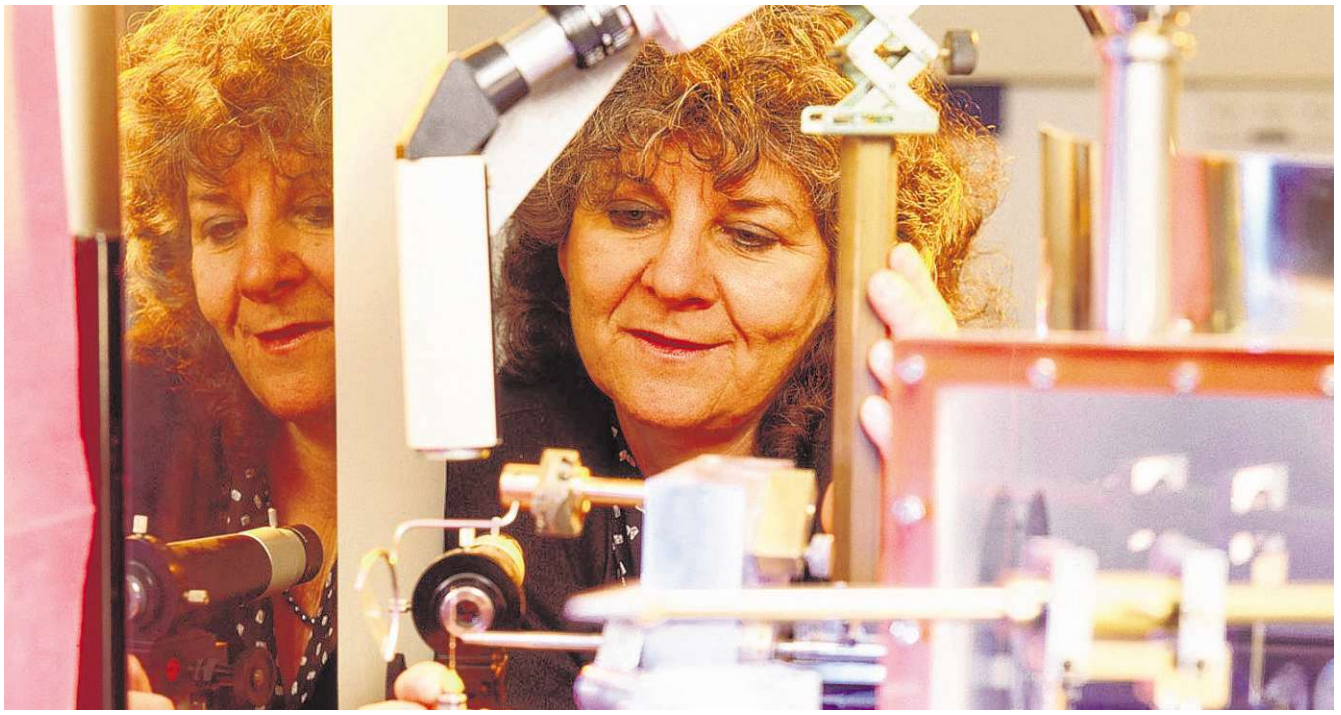
> "It is absolutely fascinating to look at how scientific discoveries become translational and find their way into the clinical sphere

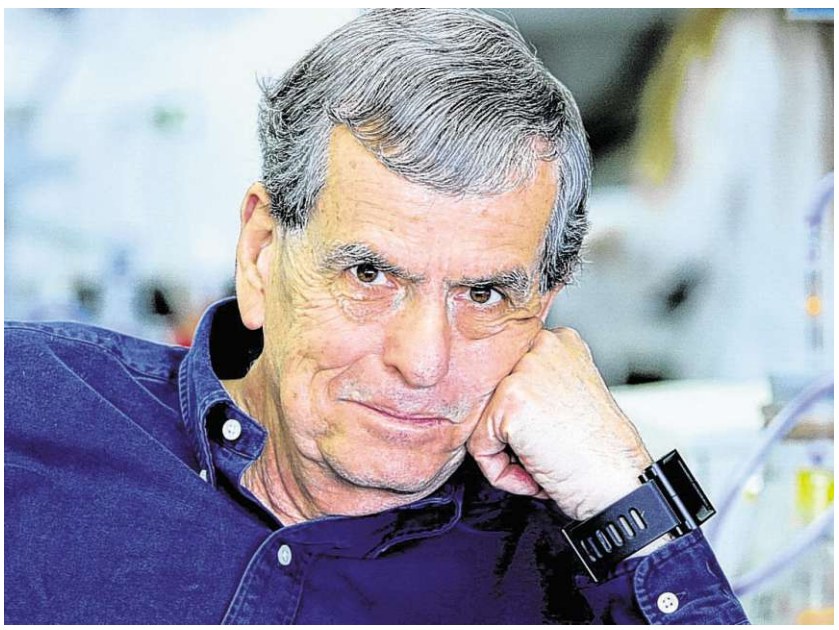
"That's what a lot of the drug companies are currently doing. In other words, instead of giving the patient a drug that will block a pathway we are looking for ways for the patient to actually generate their own anti-inflammatory response. We are trying to find ways to get the immune system to switch from being a very pro-inflammatory to an anti-inflammatory environment."

There will also be 12 speakers from Israel, not exclusively from the Weizmann Institute though. Yehuda Kamari from the Sheba Medical Center, who will be presenting The Role of Interleukin-1 in Metabolic Inflammation, is also a musician and will be playing a little Judeo-Arabic music at some point during the course of the three-day meeting.

"It is absolutely fascinating to look at how scientific discoveries become translational and find their way into the clinical sphere," he says.

"Inflammation, which is the focus of the conference, is a great example of this transition. Inflammation and specifically the innate immune system, which was mainly thought to recognize and fight external pathogens . . . turned out to be important in recognising and handling endogenous molecules especially in the context of over-nutrition and obesity. Keynote Nobel presentations by Jules Hoffmann and Bruce Beutler at the conference on innate immunity will tell us about the progress in





this field. The fascinating interplay between cellular metabolism and inflammation will also be covered, " adds Dr Kamari.

The most important focus for all attending the conference will be the science. "With two sets of people, we hope various research marriages will be inspired," says O'Neill. "The key long term goal is to get students engaged in collaborations, and translational research in order to enhance the whole science agenda."

The symposium is spread over three days with the first being a mixture of cancer and immunology speakers, including James Watson. The second day will focus on cancer and the last day is all about immunology, inflammation, and the commercialisation of research, a key area the Irish cohort hope to learn a lot about from their Israeli counterparts.

Having said that, commercial research symbiosis already exists. Another keynote speaker, Mark Feldmann from Oxford University, was behind the design of a drug used to treat rheumatoid arthritis, which is made and manufactured in Ireland by Wyeth and Amgen.

The brains behind the breakthroughs: (clockwise from top) Ada Yonath, an authority on the structure and function of the ribosome; Seamus Martin; James Watson; and Aaron Ciechanover

However, commercialisation is only one aspect. Prof O'Neill is keen to keep this as open a platform as possible.

"Obviously we need structure but were not restricting it too much," he says. "We're just aiming to make discoveries in as many areas as possible and make a difference to sufferers of cancer, motor neuron disease, arthritis, etc."

"The conference has actually been planned in such a way that we emphasize how basic science can evolve into therapy discovery, commercialisation, and business," says Wallach. "I stress 'basic science' – that is, studying not aimed to cure this or that disease, but understanding it at a fundamental level. When your body contracts a disease, its machinery goes wrong. So if you understand the machinery, you can understand the therapy."

See tcd.ie/biosciences/events

Nobel calling Confronting cancer

One of the most well-known guests giving a keynote speech at the TBSI/Weizmann Institute conference is 86-year-old molecular biologist, zoologist and geneticist, James Watson, winner of the 1962 Nobel Prize in physiology and medicine. In 1953, Watson co-discovered the structure of DNA with Francis Crick. His presentation at the conference is entitled: Cancer is a Redox Disease.

Interrupting the signals

"Redox basically refers to oxidation reduction reactions," he explains. "In addition, it relates to signals which make cancer cells grow and divide, which are frequently provided by what is called 'reactive oxygen species' or ROS. What confuses the issue is that most of today's chemotherapy produces the same reactive oxygens. So we are using ROS to kill the cancer cells too.

"But cancer cells can become resistant to chemotherapy by synthesising antioxidants. When we use chemotherapy to treat cancer, it produces mutations, which then make you resistant to the chemotherapy. Some of the most resistant cancers are so because they are filled with antioxidants so you can't kill them.

"So among other things, my talk will be about how to get rid of those antioxidants, as well as looking at any other ways to kill cancer cells. Why is so much cancer incurable and how can we get around it?

"Only one in seven non-hormonal driven (prostate and breast) major human cancers is curable. Despite all the research and everything we have tried to do, all we really have are drugs that prolong the inevitable. Eventually cancer always comes back and kills its victims.

"We also need to look deeper into anti-inflammatory solutions as inflammation is fundamental to many cancers."

Collaboration and the Weizmann Institute

"I was in the Weizmann Institute a long time ago, back in 1956. However, I have been to Ireland many times. I have an honorary degree from Trinity College, from University College Cork and one from the University of Limerick.

"I think collaboration, such as that between TBSI and the Weizmann Institute, is a good idea. Cross-collaboration is always a good idea.

"Plus the subject matter of the conference is very important. As far as I'm concerned you shouldn't do science unless you have a higher objective, unless you're doing something important. If you're not doing something important, do something else. Stopping cancer, for example, that's important. Finding cures for conditions like dementia is also important.

"When you get older you tend to think less about pure scientific questions and the fundamentals. At my age, I'm focused mainly on improving medicine."

In conversation with John Holden

Righting immunity wrongs

The Trinity Biomedical Sciences Institute and Weizmann Institute of Science are at the forefront of research into how the immune system works, writes **Dick Ahlstrom**

Some of the most important new discoveries about how the immune system works are coming out of two research centres - Trinity Biomedical Sciences Institute (TBSI) and the Weizmann Institute. The research centres in Dublin and in Rehovot in Israel are central to these developments and have embarked on a programme of collaboration that should benefit both.

Both are world players in the publication of immune system research and in both cases these discoveries are leading to new drugs and new ways of thinking about disease and its progression.

"We are working on immune cells and are following the mechanisms of these cells in health but also in disease, particularly cancer," says Prof Idit Shachar, head of the department of immunology at Weizmann and a research principal investigator.

"We are trying to understand how to control them [immune cells] and to develop reagents that will block cancer and lead to cell death."

About 100 researchers are linked with projects being run by 15 principal investigators specifically in the immune area at the Weizmann, she says.

The group is very strong in the study of autoimmune diseases. The research remit is very wide, she adds, and includes immunodeficiency, immunopathology, immunotherapy and stem-cell transplantation, inflammation, cancer immunology and autoimmunity among others.

The advances being made in our understanding of human immunity have opened the possibility of treating diseases that have always been considered intractable, says Prof Luke O'Neill, academic director of TBSI. "When immunity goes wrong it leads to a tumour. We are trying to get the immune system to wake up and attack the cancer cells."

They are beginning to see some improvements in tackling dangerous cancers such as in the lung, breast and melanoma in the skin.

The fundamental research is essential however. "The immune system is as complicated as the brain or any system you think of, and we are trying to grapple with that complexity," he says.

There are about 120 immunology researchers working in the Trinity institute, led by 12 principal investigators, a research team that he describes as "a good critical mass".

In common with research centres around the world, the goal is not just to make discoveries but to turn them into better patient treatments and new drugs as quickly as possible.

There are spectacular examples of this, for example Weizmann's central research contribution in the development of the multiple sclerosis drug Copaxone.

Another is Marc Feldman's discovery of anti-TNF therapy as an effective treatment for rheumatoid arthritis and other autoimmune diseases, leading to drugs such as Enbrel.

These drugs represented a huge advance when they came into use but they have their limits. "These drugs don't cure, they slow the disease down so we still have a way to go. But this is the direction the research is heading," says O'Neill.

Leading the way at Trinity are scientists such as Kingston Mills, who is studying whether vitamin A could be used to limit the damage caused by inflammatory bowel disease; Padraic Fallon, who has found genes associated with eczema, and O'Neill himself, working on inflammatory diseases and their control.

Immunology research: a time of hope and optimism

These are exciting times in immunology research, with strong signs that using the body's own immune system may begin to deliver better medical care.

"It is so exciting, all the breakthroughs that are happening and beginning to improve treatments for patients," says O'Neill.

"There is a big hope, without overhyping it, and there is real optimism."

His upbeat view comes from the range of immune system discoveries being made at centres such as the Trinity Biomedical Sciences Institute, where O'Neill is academic director, and at the Weizmann Institute of Science .

"The key message is dysfunction of the immune system is behind every disease."

He includes among these arthritis, Crohn's disease, asthma, Alzheimer's disease, multiple sclerosis, motor neuron disease and others.

"It is the immune system that has gone rogue in these diseases. We are trying to unravel the component parts of the immune system in the hope of developing new drugs and better patient care."

Research in this area at the Weizmann Institute has already delivered breakthrough drugs, for example the development of the MS treatment Copaxone by Michael Sela and Ruth Arnon ,says Shachar, the head of the department of immunology.

She too is upbeat about developments in the field and the positive impact they are likely to have with improved treatments.

"The Weizmann is recognised for its excellent science. We are very independent and have our own sources of money. This makes us an attractive place," she says.

"We believe in the future."

How to fight a virus

Prof **Cliona O'Farrelly** on super 'innate' mechanisms and why some immune systems work more powerfully than others.

Why can some people tolerate a virus while others get sick from it? It's a question of interest to Prof Cliona O'Farrelly, whose work at the TBSI looks at the Hepatitis C virus, or HCV. "Some people can live almost normal lives while chronically infected with HCV, while others develop such serious liver disease that they have to have a liver transplant," she explains.

Prof O'Farrelly, whose research has built up our understanding of how the immune system functions in the liver, works with samples donated by women who were exposed to HCV through infected blood products.

"At the moment we are interested in women who were exposed to the virus and yet never made antibodies, which suggests they tackled the virus another way," she says.

The answer could lie in the women's "innate" immune systems, where immune cells in the body may have squashed the virus before there was even a need to make antibodies against it, explains Prof O'Farrelly.

"We think they have 'super' innate immune systems that can protect them from viral infections, so we are now looking at the genes that could be involved."

Understanding the frontline mechanisms that work against viruses would offer clues about how to boost those defences, according to Prof O'Farrelly, who is professor of comparative immunology at Trinity. "We might ultimately be able to design successful vaccines against HCV and perhaps other viruses where we have no vaccine, like HIV and the cold virus," she says. "And these discoveries would be important for regulating important viral infections in other species, such as foot-and-mouth disease and avian flu."

Prof Cliona O'Farrelly: her research aids our understanding of how the immune system functions in the liver

A triumph over inflammatory diseases

Prof **David Wallach** made a discovery that led to new drugs to relieve rheumatoid arthritis

Discoveries in the lab can transform the way disease is treated. One such breakthrough was working out how, at a molecular level, damage is triggered in diseases such as rheumatoid arthritis and other chronic inflammatory conditions, and, importantly, how to block that damage.

Prof David Wallach, who holds The Joseph and Bessie Feinberg Chair at the Weizmann Institute's department of biological chemistry, played an important role in discovering how members of the TNF family of biological molecules function in the body and how they can cause damage in inflammatory disease.

Wallach and colleagues also discovered the so-called "soluble TNF receptors", which are made by the body itself. "These molecules prevent excessive function of TNF," he explains. "We discovered the soluble TNF receptors by following our hypothesis that nature normally takes care to restrict the function of TNF and thus prevent the development of chronic inflammatory diseases."

Prof David Wallach: his lab is continuing to explore the TNF family

The researchers reckoned that the soluble TNF receptors they harvested from human urine might be a useful basis for therapy, according to Wallach.

They were right – the research, which spanned three decades and was supported by the pharmaceutical company Serono (since merged with Merck), paved the way for new treatments of conditions such as psoriasis, psoriatic arthritis and rheumatoid arthritis (a drug developed as a result is produced in Ireland). It also helped to seed the new wave of "biologic" drugs that use antibodies to target chronic inflammatory conditions.

His lab is now further exploring the functions of the TNF family. It provides plenty to work on, notes Wallach. "Having evolved over many million of years, the TNF family also exists in anemones, sea-urchin and flies, these molecules and mechanisms might well need several hundred of years of research to be fully deciphered."

Improving transplant efficiency

Prof **Yair Reisner** is working to counter an issue of for bone marrow transplants in leukaemia

Soybeans might seem like unlikely saviours in the field of bone marrow transplantation, but they played a pivotal role in helping to overcome the issue of needing to find a matched donor to avoid the transplant being rejected by the recipient's body.

Three decades ago, Prof Yair Reisner, who is the Henry H Drake professor of immunology at Weizmann, and colleagues showed that soybean molecules called lectins could be used to remove rejection-triggering T cells from bone marrow before it was transplanted into non-matched mice.

Such "T-cell depleted" transplants translated successfully into treatments for so-called "bubble children" whose own immune systems had been wiped out by severe combined immunodeficiency (SCID), explains Prof Reisner, who is the Henry H Drake professor of immunology at the Weizmann Institute. "This approach for the treatment of SCID was adopted by many centres throughout the world with impressive long-term survival," he says.

Prof Reisner has also focused on an issue for bone marrow transplants in leukaemia: that small numbers of residual T cells in the recipient can trigger rejection of a transplant coming in. He discovered in a mouse model that bombarding the recipient's immune system with large numbers of stem cells in the bone marrow transplant could help to overcome this barrier.

"It established the principal that elevated stem cell doses, known now as a 'megadose', can improve the efficiency of the transplant," says Prof Reisner, who is continuing to work on the approach so it may be used more effectively in humans.

Prof Yair Reisner: "Elevated stem cell doses can improve the efficiency of the transplant."

Fishing out clues about our response to viruses

How do cells know they are under threat? Prof **Andrew Bowie** is baiting them with viral DNA to find out

Some viruses can cause illness if they get inside your cells and start making copies of themselves. To mount an immune response against the virus, a cell needs to know the intruder is present and sound the alarm – but how does that happen?

Prof Andrew Bowie, who is professor in immunology, is doing a spot of fishing to find out. His lab sends chunks of viruses into cells to see how the cells react.

"One of the key things that cells respond to, to sense invasion by a virus, is the presence of viral DNA inside an infected cell," says Bowie, who is a professor in Trinity's school of biochemistry and immunology.

"So we went 'fishing' inside the cell by using viral DNA as a 'hook' to catch a big fish - namely a brand new viral receptor in cells, called IFI16. Further work showed that what we caught was really important, since many other labs have now shown that numerous types of viruses, including HIV, are sensed by IFI16, leading to anti-viral and immune signals being turned on."

Now that Bowie's lab has identified this DNA sensor, the TBSI researchers are looking at how the cell switches on the anti-viral arsenal when has sensed that the virus is lurking. Plus they are doing some more fishing. "We are undergoing more fishing expeditions inside cells, this time with viral proteins that we know can switch off the anti-viral and inflammatory signals," he explains. "This allows us to fish out human proteins targeted by the virus, which very often gives us a lot of new information about how the human anti-viral machinery functions."

Gone fishin': Prof Andrew Bowie

Prof Padraic Fallon: "The TBSI network enables scientific discovery." PHOTOGRAPH: DAVID SLEATOR

Finding 'rogue' genes in eczema

A gene whose mutation is linked with dermatitis has been found by Prof **Padraic Fallon** and his team

Why do some people develop eczema while others don't? TBSI researcher Prof Padraic Fallon is finding out by looking for "rogue" genes associated with the inflammation of the skin.

"People of Irish descent are genetically highly susceptible to atopic dermatitis, commonly called eczema," says Fallon.

"The immune system merges the influences of the genes that predispose to allergies and the exposure to environmental factors that can lead to the allergy. So if we can understand how and why the immune system causes diseases, such as atopic dermatitis, we can develop new strategies to prevent or treat allergies."

Fallon and his colleagues have identified a gene called Matt, in which mutations are linked with dermatitis. "This is a new discovery, raising the potential to screen patients for mutations that may lead to atopic dermatitis," he says.

His work has also shown that the flare-up of inflammation in eczema involves an immune cell called ILC2 – a type of cell that Fallon and colleagues described for the first time in 2011. "These discoveries will impact on future treatments for atopic dermatitis," he says.His is now exploring why some children who have eczema develop asthma while others do not, and why some children "grow out of" their allergies. "These are fundamental questions for improving patient health and reducing the socio-economic impact of these conditions in the long term."

> "If we can understand how and why the immune system causes diseases, we can develop new strategies to prevent or treat allergies

Fallon, professor of translational immunology at Trinity, believes the TBSI is an ideal environment for discovery and creating new paradigms in science.

"TBSI is a 'perfect storm' of both outstanding scientific personnel and world-class infrastructure," he says. "In short, the TBSI network enables scientific discovery."

Vitamin A could be for immunity

Tests bore out Prof **Kingston Mills'** hunch that vitamin A could aid inflammatory bowel disease

Prof Mills: 'Retinoic acid reduced clinical symptoms of colon inflammation.' PHOTOGRAPH: DAVID SLEATOR

Could something as simple as vitamin A help protect against inflammatory bowel disease? It's an idea that Prof Kingston Mills, a professor of experimental immunology at TBSI, has explored with promising results.

Based on previous work in his lab, on how a breakdown product or "metabolite" of vitamin A, called retinoic acid, helps regulate the immune system, Prof Mills wondered whether retinoic acid might have an effect in Crohn's disease, a chronic autoimmune disease in which the inner lining of the gut becomes inflamed.

"Since chronic inflammatory and autoimmune diseases are often caused by a defect in immune regulation, we had the idea that giving the vitamin A metabolite might be beneficial in treating inflammatory bowel disease," he says.

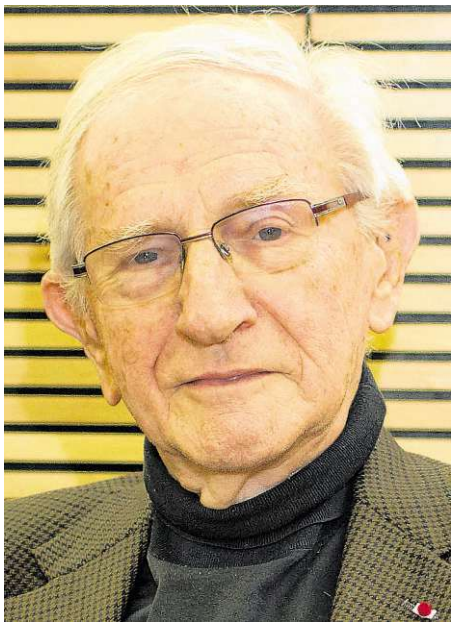
His hunch was right, in a mouse model at least. "We found that administration of retinoic acid reduced the clinical symptoms of colon inflammation in mice," says Prof Mills, who is Professor of Experimental Immunology at Trinity.

His research showed that retinoic acid acts on immune cells in the intestine that produce a protective molecule, which buffers the intestine against damage caused by bacteria in the gut.

Vitamin A supplementation is already being used in various trials involving humans that look to tweak the immune system, and Prof Mills's results help explain its effects. In the meantime, there are more practical steps we can take to help keep our immune systems in balance, he says. "Our findings provide evidence for the health benefits of eating a diet rich in green and root vegetables."

A career shaped by molecular synergy

Prof **Michael Sela** extensive career continues to give insights into the importance of the structure of molecules



Former president of the Weizmann Institute Prof Michael Sela

Your body is made up of tiny molecules. The shape of each molecule is extremely important, because it determines how it can interact with other molecules, and these molecular "conversations" are what make your body work.

Prof Michael Sela, the W Garfield Weston professor of immunology at the Weizmann Institute, has made profound contributions to our understanding of how the shapes of molecules in the immune system, called antibodies, are determined, and also how to use antibodies as medicines.

One of his major achievements was to show, almost 60 years ago, that the shape of proteins is under genetic control and that this goes for antibodies too.

Then, more than 20 years ago, he and colleagues demonstrated the synergistic effect of using a combination of an antibody and a small chemotherapeutic drug in fighting cancer. "This in turn led to the discovery of the synergistic effect of two antibodies against the same receptor for treating experimental cancer," he says.

Sela cites his most rewarding discovery as one he made with Prof Ruth Arnon, also of the Weizmann Institute, that led to the development of a major drug used to address multiple sclerosis. "Both the [DRUG]against MS and the synergistic effect against cancer became blockbusters in the pharmaceutical industry," he says.

Now 90, the former president of the Weizmann Institute is still actively involved in research. "I have been working in recent years with Yossi Yarden on the antibody combination approach for pancreatic cancer," he says.

Leukemia and B-cell blocking

Prof **Idit Shachar's** work is focused on the adverse effect a specific protein has on leukemia patients

Your immune system is there to protect you, but if it gets out of balance it can itself become diseased. B-cells are a case in point. These protective lymphocyte cells of the immune system help to fight off infection and, like other cells in the body, they typically die off and are replaced over time.

However, in a form of cancer called chronic lymphoid leukemia (CLL) the B-cells don't die off as normal and the body ends up with too many of them.

"In healthy individuals, the pool of peripheral lymphocytes is constant in size as a result of a very fine balance between lymphocyte production, survival and proliferation," explains Prof Idit Shachar, the incumbent of the Dr Morton and Anne Kleiman Professorial Chair at the Weizmann Institute. "A hallmark of CLL is increased survival of B-cells, resulting in the accumulation of malignant cells."

Her work at the Weizmann Institute is uncovering why the B-cells don't die off as normal in CLL and she is homing in on a particular protein in the cells.

"Our research has shown that activation of this specific protein, CD74, in the B-cells in CLL patients initiates a chain of reactions that contributes to the abnormal survival capacity of the CLL cells," explains Shachar. "Our progress in locating and understanding these B-cell survival signals in CLL resulted in the development of a targeted treatment to block the cell's survival receptor and ultimately cause the cancer cell to die."

Shachar is now collaborating with the pharmaceutical industry with a view to developing the approach as a clinical drug.

Science teaching for the future

The TBSI and Weizmann Institute of Science both have renowned research profiles, which run alongside highly regarded education programmes, writes **Peter McGuire**

A new treatment for cancer. Breakthrough in genetic testing. World's smallest camera invented. It's the big research that grabs the headlines. But this research would simply not happen without the education that trains every generation of scientists.

The Weizmann Institute of Science and the Trinity Biomedical Sciences Institute (TBSI) both have renowned international research profiles, which run alongside a suite of postgraduate and undergraduate education programmes.

Weizmann is a rather unusual beast, says Prof Irit Sagi, dean of the Feinberg Graduate School at the Weizmann Institute. "We have no undergraduate students, only master's and PhD candidates.

"The idea was to create an elite institute focused on basic research across five faculties. We encourage interdisciplinary science, with students and principal investigators interacting on both a formal and informal basis. This, along with visiting scientists from all over the world and a number of postdoctoral researchers, creates a unique scientific atmosphere on campus."

The Feinberg Graduate School was founded in 1958 to train future leaders in science, with English as the language of instruction.

Studies are conducted within the framework of five research schools – physics, chemistry, life sciences, mathematics and computing, and science teaching.

The institute has a special programme for master's students, who enter after a rigorous screening programme. After one year, students choose a mentor and pick a research topic based on an area of interest. They also get to spend 10 weeks working in one of the world's best research labs with a principal investigator.

All students are directly involved in the research conducted at the institute. At Trinity College Dublin, meanwhile, there is a formal link between the TBSI and five heads of schools: biochemistry and immunology; chemistry; bioengineering; medicine; and pharmacy and pharmaceutical science.

Prof Luke O'Neill, academic director of the TBSI and professor of biochemistry, explains: "Each school has staff working in the TBSI and the heads of school sit on our management group. This presents opportunities for interdisciplinary learning, because it gets people from different disciplines talking to each other and learning from each other. We have had over 60 publications describing discoveries based on these interactions so it is starting to work."

The TBSI, like the Weizmann Institute, is focused on postgraduate education, offering both PhD and MSc programmes across all aspects of biomedical sciences.

The MScs include immunology, translational oncology and bioengineering. Last year, 40 per cent of the TBSI's PhDs went into industry. "They are a key resource for Irish industry, while the rest are doing further postdoctoral research or may have left Ireland to continue in research," says O'Neill.

Undergraduates are nonetheless important to the TBSI. "The jewel in the crown of our undergraduate degrees is that, in final year, students do a real research project and get to see what it is like to be a research scientist."

The TBSI's suite of education programmes, and its teaching and learning, has changed significantly over the past decade. "We have introduced several important new aspects so that students can get such skills as entrepreneurship, communication skills, including making presentations and written skills, and a range of other transferable skills," says O'Neill.

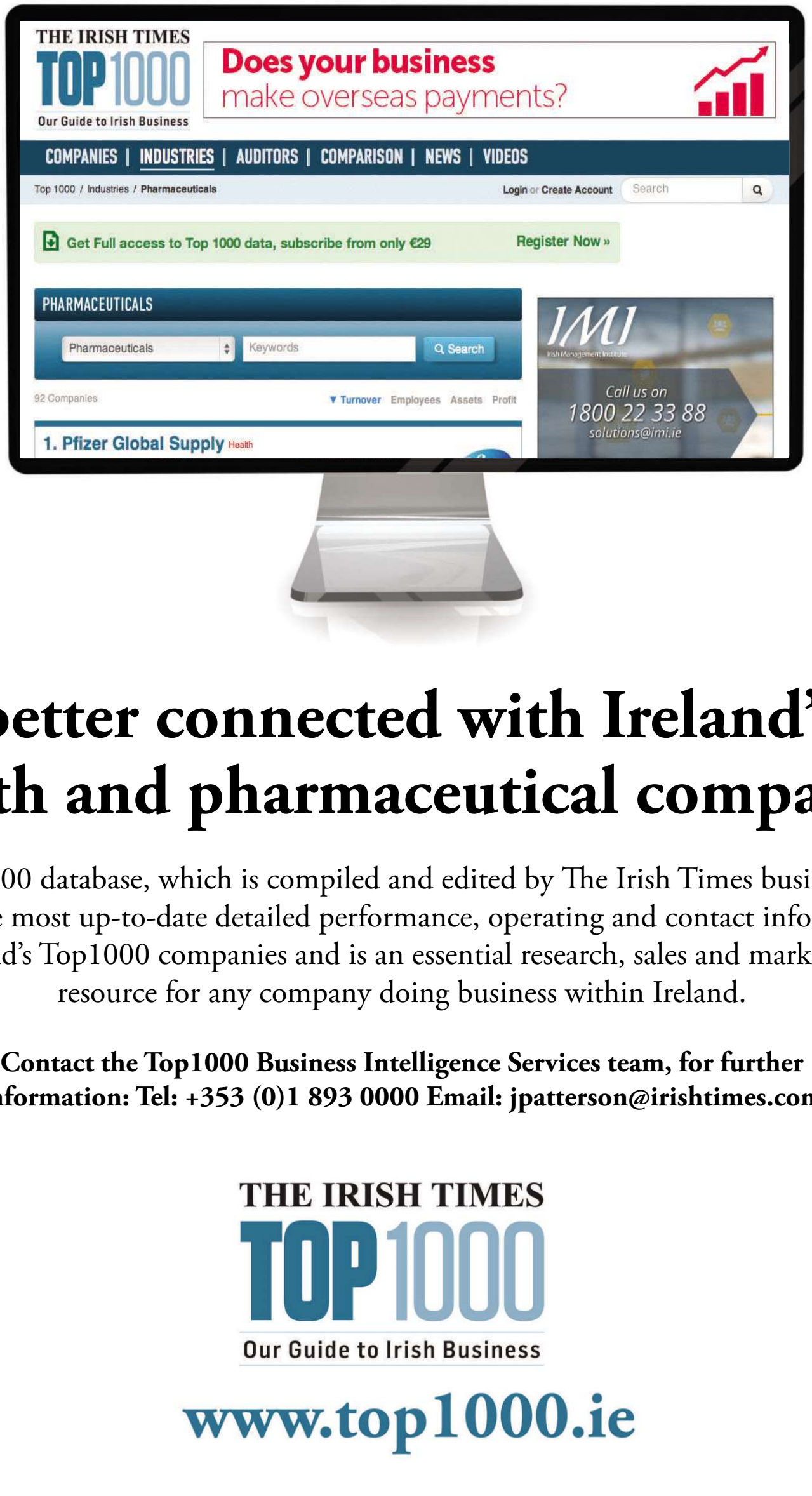
"Not all of them will end up as research scientists so we have to prepare them for the world of work. Having a science-based degree means they are in high demand because of the exacting nature of science and the fact that the best jobs are and will increasingly be in science and technology."

> "Ultimately, good science cannot exist without good science education, and this is where we are making a real difference

Technological space: Science Gallery, which is closely linked to the TBSI, hosts creative and innovative exhibitions that explore human aspects of scientific phenomena

The educational remit of both the TBSI and the Weizmann Institute extend beyond teaching their own students. The TBSI is closely linked to the Science Gallery, a space in Dublin where scientific ideas are expressed, explained and presented through art installations. It has become an important tool for communicating big ideas in science to a younger generation.

Weizmann, meanwhile, has the Davidson Institute, which aims to make science accessible to the general public through lectures, talks and an innovative "Garden of Science", which allows the public to meet Weizmann's scientists. The Davidson Institute also brings schoolchildren to Weizmann for day trips or longer stays, during which they get a chance to conduct science experiments in high-tech labs."Weizmann has a tradition of over 50 years of education," says Avi Golan, head of the student activities unit at Davidson. "Ultimately, good science cannot exist without good science education, and this is where we are making a real difference."



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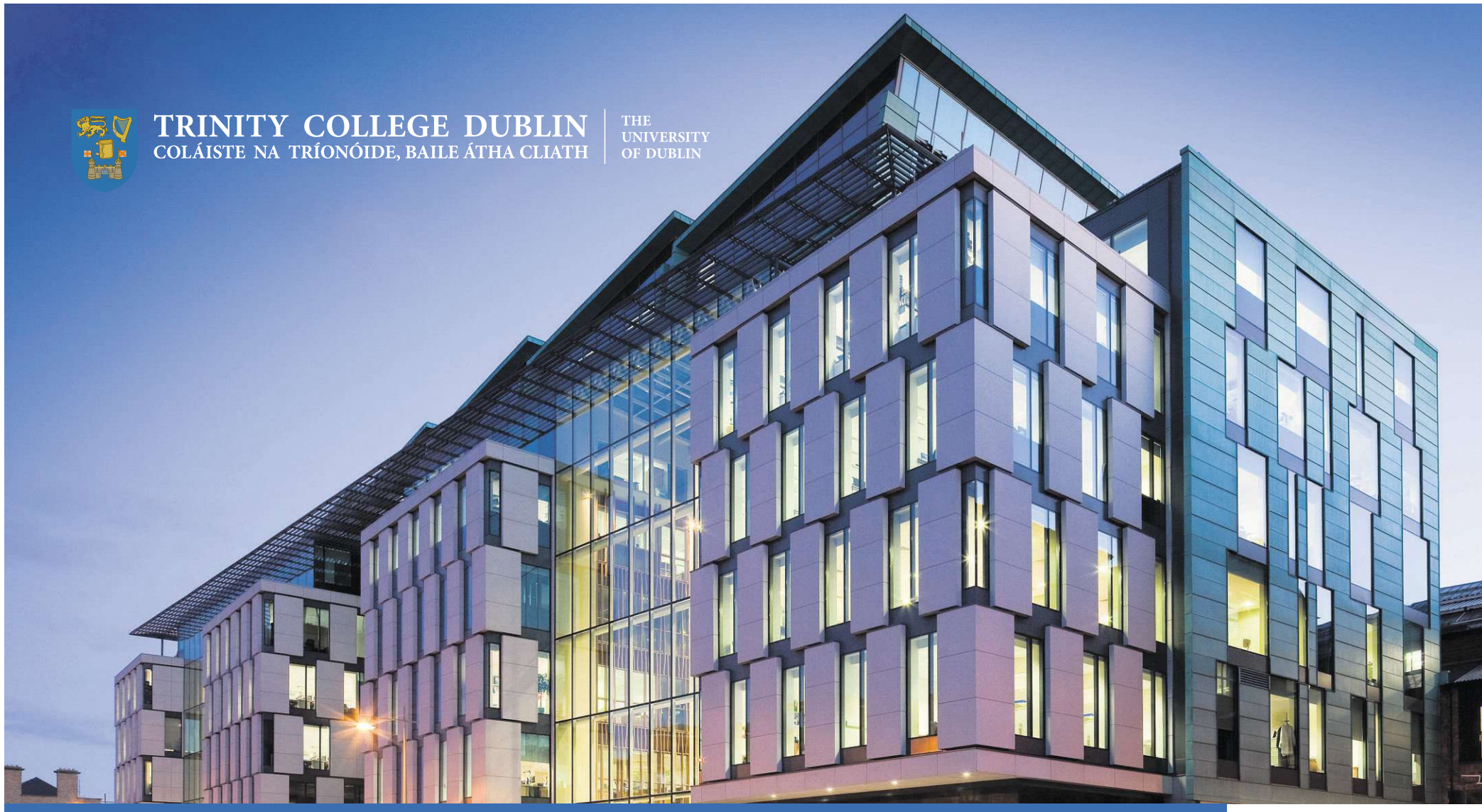

TRINITY COLLEGE DUBLIN
COLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH
THE UNIVERSITY OF DUBLIN

MASTERS PROGRAMMES AT TRINITY BIOMEDICAL SCIENCES INSTITUTE

Apart from undergraduate and Ph.D. studies, there are two new masters programmes available at TBSI:

M.Sc. in Bioengineering

The M.Sc. in Bioengineering is a full-time one year course which aims to provide engineers and scientists with the education and creative skills needed to practice in the medical devices industry in Ireland. It consists of taught modules and a project focussing on medical devices and important clinical needs.

The only course of its kind in Ireland, the M.Sc. in Bioengineering received two awards in 2012 which recognise the scale and diversity that the M.Sc. in Bioengineering course delivers in terms of the student experience, its contribution to the Irish economy and its impact on global healthcare challenges.

Now, in addition to the award winning M.Sc. in Bioengineering programme, students can opt for the M.Sc. in Bioengineering with specialisation strands (Neural Engineering, Tissue Engineering or Medical Device Design). All four streams lead to the award of the M.Sc. in Bioengineering and consist of compulsory core modules and optional modules.

Contact: June O'Reilly; Email: tcbe@tcd.ie ; Tel. +353-1-896-4214

M.Sc. in Immunology

This 12 month full-time course is designed for graduates aiming to pursue careers in academic research, medicine or the pharmaceutical industry for which a thorough grounding in immunology, immune-mediated pathogenic mechanisms and immunotherapy is required. The course is underpinned by modules in basic immunological principles and technologies. A key component is the twelve week research project to be undertaken by each student under the supervision of an academic staff member.

Contact: Course coordinator: Dr. Nigel Stevenson;
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