MTC NEWS

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The MTC Social Circle

Hahahaahahaha!! On the cover of MTC News again. First I will take MTC news then I will take over the prefecture. Thanks to my friends at the korvkiosk, they are mixing arsenic in the Klas' Bostongurka. Soon, soon my little pretties!!!! Ooops have I been writing out loud again?

And now for something completely different. Well I was meant to get a report on Andreas Mörner's thesis party but I guess we will have to wait until next month. So then the most social thing was the MTC Christmas Party. This year it was coordinated by Francesca Chiodi and once again she and her crew must be heartily congratulated for a job well done. Unfortunately, due to other commitments I came late so had to sit far from the action and the sound of the speaker so I could not hear everything that went on at the beginning. However Santa Claus was once again able to come down from Tomtebodavägen and distribute gifts to all those deserving (i e not me!!). Then came the MTC film, "Kärre's Angels".

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HOW IT WAS DISCOVERED

THE DISCOVERY OF EBNA

Sometimes in the mid-sixties, I went to see John Moloney at the National Cancer Institute. John was an old friend but he was now also the Head of the Virus Cancer Program at NIH. They have given out contracts to many labs, including our own, to "speed up" what came to be known as Richard Nixon's "War on Cancer". Part of our contract was concerned with Burkitt's lymphoma (BL). Guided by our experience on virus induced murine leukemias, we wanted to trace new membrane antigens, encoded by a suspected but unknown virus, presumably carried by Burkitt lymphoma cells. We have established a weekly "air link" with an ENT surgeon, Peter Clifford, at Kenyatta National Hospital in Nairobi. He was sending us BL and other African tumor biopsies and sera every Tuesday with the weekly SAS connection.

Entering John's office, I happened to run into Tony Epstein, another old friend since the 50s when he was doing electron microscopy on cancer cells and used to visit Torbjörn Caspersson's laboratory, where I worked. Now he came to show five or six electron micrographs with large, conspicuous round particles in some cells.

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Social Circle *continued*

It had been 3 years since the last MTC film so it was not surprising (although surprising to me) that some people had not seen the previous films. In fact, this year's film was last year's film. Last year in postproduction, i.e. 30 minutes before viewing, a file got corrupted and destroyed everything. However this year after making multiple back ups and completely digitally remastering the film and adding new scenes, the directors cut was released. This film had it all. It made me laugh, it made me cry, and I sat on the edge of my seat with the suspense (even after seeing it over 50 times). However, as the fourth film of the Spice Scientist trilogy (along with The MTC Full Monty, MTC Robinson and MTC Star Wars, the funniest of them all until the film got destroyed in the camera), it appears that this will be the last Spice Scientist movie. So now a whole new series will probably begin, although for some reason I think that some of the main characters will be in the next film too. However for those of you who are interested in how an MTC film is made a documentary entitled "The Spice Scientists Golden Years" is apparently being planned with interviews, out-takes and actually rare unseen footage of the script writing. It is hoped that all the MTC films made to date will be available on CD sometime soon.

After the film came the Salsa. Many hips were a turning and the uncoordinated became coordinated. That was unless they had been influenced by some of the beverages being offered by the bar. The Salsa extended into the disco, where all the good work from the Salsa disappeared as the bar's beverages began to take hold. Despite some hiccups, the music on the whole was good and danceable (even the old people were dancing!!!). I left at 2.00 am to write this article but I am informed that the party did go on the wee small hours.

And so it is now 2002!!! Plans are afoot to improve the social life of MTC with social events once coming again periodically at MTC. Hopefully the new Sven Pettersson people will inject some life as they did at their house warming party. Until next time party hard and vaya con Dios!

Benedict Chambers

CHAIRMAN´S CORNER

Dear MTCers,

This is the first issue of MTC News 2002, but the year is already more than one month old. It has been a month characterized by intensive activities. Several deadlines have passed, and on behalf of MTC I have had the pleasure to sign many excellent applications for grants, positions and permissions to defend a thesis. Our new seminar series has started, and one can already notice an increased number of listeners as well as a higher intellectual temperature in A302 between 13.00 and 14.00. We thank our new seminar leader teams and wish them good luck in the months to follow!

Our reformed course in Medical microbiology for medical students has just reached halftime. It will be interesting to see the evaluations of the course, but as one of the teachers, I would like to make some spontaneous comments already now. For those of you who know less about this, let me first mention two new aspects (see also articles in previous issues by Monica Thelestam and Roland Möllby, or contact them for a demonstration). The microbiological subdisciplines and immunology are now integrated throughout the course. Furthermore, it is based on a web platform where a lot of the course material is accessible as e g lecture abstracts, links to interesting sites, reference literature etc. There is also an electronic discussion forum. I find it very stimulating to being able to see what other teachers have (or plan to) discussed with the students and on the basis of this, interact by mutually adjusting lectures, exchanging slides electronically etc. It is even more stimulating to communicate with the students on the ”discussion forum”: to get a question, answer it in a way that leads to front line research and ask the student to reflect further and suggest an interpretation or an experiment, and then a few days later actually get very smart suggestions back. Your attitude to medical

students changes dramatically! These are just some spontaneous comments as a teacher, and we must of course await the evaluation by the students, and also by teachers in later courses in Clinical microbiology and Infectious diseases. We will then discuss whether we should go in a similar direction also in other undergraduate and graduate courses. I remind you that teaching is one of five strategic areas defined for the present development of MTC.

Strategic Areas

1) Teaching, 2) Information, 3) Quality improvement in the interface between academic and technical / administrative staff, 4) Recruitment to tenure track positions. 5) Networks and alliances for graduate programs and broader research projects.

Another such strategic area is recruitment of scientists at the group leader level. Looking at 2001, this has been most obvious in the area of bacteriology. Three new positions have been established mainly through external and KI funding, and a fourth will be decided soon through funding from SMI (the professorship in Clinical bacteriology within Infectious disease control). It is now time to intensify the efforts in our other areas, primarily Tumor and cell biology and Virology, and this will be a top priority for 2002.

Finally some words about a third strategic area: quality improvement in the interface between academic and technical/administrative (TA) staff. Our ambition for the common MTC T/A staff group under Claes Fritsch should be as high as our ambitions for the research groups. It should function and interact as a group, with internal collaborations and backup, and the best external contacts towards our research groups, the KI administration, companies delivering or collaborating with MTC, recruitment agencies etc. The group is organizing and developing itself through various measures right now. Please bring your suggestions if you see areas for improvement. The forum for interaction and influence by all staff groups at MTC is the Department Council (Institutionsrådet).

DEPARTMENTAL COUNCIL

Chairman	***Mandate up to***
Klas Kärre	2002-12-31
Secretary	
Anita Wallentin	
Regular members	
Teachers	
Mikael Jondal	
Marta Granström	
Victor Levitsky	
Roland Möllby	
Britta Wahren	
Anders Örn	
TA Staff	
Elisabeth Kaven	2003-12-31
Margret Wahlström	2002-12-31
Laboratory Staff	
Berit Olsson	2002-12-31
Birgitta Wester	2003-12-31
Grad. Students	
Anna Berg	
Stefan Ternen	
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Vacant	
Coopted administrative issues	
Irene Hemmingsson-Klang	
Claes Fritsch	
Coopted information issues	
Marie Bohm	
Coopted student representative	
Vacant	

We have recently defined the tasks of this council in a sharper way, and will actually let it take primary responsibility or come in first on the scene for certain issues. These include among other things information (a fourth strategic area for MTC), common MTC activities such as retreats, introductory programs for newcomers, appointments of certain important assignments. In the latter context, it has just appointed Mikael Rhen as new Biosafety Officer, and Ingemar Ernberg as new representative for issues relating to equal opportunities (including the aspects of gender, nationalities, culture etc). We wish them good luck, and we thank the previous persons on these posts, who resign after more than two years: Franscesca Chiodi and Ann-Beth Jonsson. If you wish to raise issues in the Department Council, please contact one of your elected representatives.

Klas Kärre

New colleague in IT support!

On Monday the 18th of February we welcome Eric Björkvall as IT Manager ("IT-samordnare") at MTC.

Eric is a well-known person at MTC, as he has – as a consultant – been supporting the local Macintosh networks for several research groups within the department for a number of years.

Eric is a civil engineer, educated at The Royal Institute of Technology ("KTH") in Stockholm. After he had finished his undergraduate exam, he started as a PhD student at the Department of Biochemistry under professor Mathias Uhlén. Eric's research area was automatic PCR-sequencing with robots and image analysis software. However, this computer-intensive work gradually moved him away from biochemistry into the world of computers. For example, Eric became responsible for all of Biochemistry's Macintosh computers, and soon he started his first company.

After two years of graduate studies, Eric left KTH and started as a System designer/programmer at TV4 AB, taking care of - and developing – a mission critical scheduling/booking database. Eric liked it at TV4, but he soon started to long for the academic world again. In 1998 he therefore accepted a position as system engineer to build up the computer environment for a new education at KTH – "Affärsutveckling och Medieteknik" – from scratch.

Eric has a great deal of experience both from the PC- and MacIntosh platforms, and he is a member of the exclusive club that – no matter what the majority (including the Head of Administration) thinks of the future for MacIntosh – by heart has chosen Mac as his preference. As Alex Feldötö has chosen the PC-platform as his preference, Eric and Alex has decided that Eric is the first natural contact for Mac-support, and Alex the first contact for PC-support. But the ambition is, naturally, that both Alex and Eric shall be able to fill in for each other.

Eric has run several different companies while being employed at KTH and TV4, and he started to do this full time at the beginning of 2001. As MTC soon became one of his largest customers, he knew that he could get on well with the colleagues and the environment at the department. Therefore, he didn't hesitate to accept the position as IT Manager when given the offer. He has told me that he has many plans on how to make the IT environment at MTC more efficient – so, welcome, Eric! and prove to be the asset I know you can be!

New co-worker in the EA-support group

Annika Rameborg has finished her trial employment at the EA support group. The main reason is that she from the beginning has been ill in bed and therefore not able to show from her best. We wish Annika a soon recovery and good luck at her next employment!

We hope to have a new employee in her place very soon.

Claes Fritsch
Head of Administration

COOKING AROUND THE WORLD

Colombian Cuisine

Colombian cuisine results from the mixture of indigenous as well as West African and South-European culinary traditions. Raw materials originally found in the Americas have been creatively mixed with food stuff imported by early immigrants. The resulting cuisine is very characteristic to our part of the world. Unfortunately for nostalgic Colombians, it is not easy to find in Europe, and even less here in Scandinavia. We have dishes particular to each region of the country: fish and coconut are favoured on the Caribbean and Pacific coasts, while in the Andes mountains we lean more toward beef, chicken and pork. The main food staples are, however, potatoes, rice, plantains, beans and cassava, meat generally being more of a luxury. I might add that, in answer to an often-asked question I get, it really has very little in common with Mexican food! The following recipes I present are devised for people who, unlike me, like to do things in a kitchen. Gastronomically removed from French refinement or snobbery, this food item is very popular and typical in my region of origin, being prevalent in all food stands. Though it always tastes good, its manufacture requires some coordinated manoeuvres in the kitchen. As a reward, this is as close as you can get to being a real gastronomic back-packer.

Papas rellenas con salsa de ají (stuffed potatoes with ají-sauce)

Papas rellenas: Ingredients: 5 middle-sized potatoes, 100 grams ground beef, 1 hard-boiled egg, 1 onion, 1 red tomato, salt, pepper, cumin, vegetable oil. For the batter: 1 raw egg, 2 tablespoons of wheat flour, 2 dl milk. Preparation: Cook the peeled potatoes in water with salt until they are very soft and crush them with a fork, making purée. Meanwhile, stir fry in a little oil a mix of finely chopped onion and tomato until golden, then add the beef and cook until meat is well done, adding pepper, cumin and salt at will. Chop the hard-boiled egg and add it to the meat. In a separate bowl, beat the raw egg, then add flour and milk until you obtain a soft pancake-batter quality. With your hand, make potato balls the size of a small fist, dig a hole in the middle, fill up with the meat stuffing, and close it again. Heat frying-oil in a pan deep enough so that it covers the potato balls. Dip these into the batter, impregnating all sides, and then put in the oil when it is hot enough to fry a drop of batter (but not too hot!) Leave until golden on all sides. Absorb excess oil with paper towels. Eat hot or cold.

Aji: Ingredients: 1 red pepper (paprika), 1 small chilli pepper (only if you like hot and spicy sauces) 1 garlic tooth, 1 dl lime juice, 1 cup with 2/3 water and 1/3 white wine vinegar,1 green onion (or a scallion), a handful of fresh coriander, salt, pepper and oregano. Mix all ingredients (except the onion and the coriander) into the blender until homogeneous. Finely chop the onion and the coriander and add it to the mixture, add the spices to your liking and mix with a spoon. It keeps in the fridge for several days. Put on top of the potato and enjoy.

Silvia Botero

***Footnote**: the recipe shown in the photo is too complicated to be given here, it is, nevertheless, delicious, as well as filled with calories. It also looks terrible in black and white.*

Student Board News

The Student Board have asked the Prefect whether he would present the **New Rules for PhD students at MTC**, as it was formulated at the end of last year. It concerns all students of the new regulation, i.e those of you registered **after** April 1st 1998, but I suggest that also the "elder" students come and listen to what MTC request of their students and what the students can, in return, demand from the department. The Prefect has promised to set a date for this meeting, which will be announced after February 22nd. In the meantime, you could check the web at http://www.ki.se/org/df/Financing_rules.htm for some general KI guidelines. Or surf our MTC intranet for the specific MTC "handbook of rules" at http://www.mtc.ki.se/education/graduate/handbook_01.pdf.

The next **Student Board meeting** will thus take place some time after the 22nd of February, probably in the early (and hopefully sunny & warm) days of March.

All students registered within the **Tumor Biology & Oncology program** here at KI are hereby kindly asked to think about what would be the ideal settings for a big "get together", as there are plans to arrange a meeting after the summer for all PhD students, and supervisors, within this field. We would like for all of you to get to know one another and to possibly learn more about other tumor biology projects that are going on at KI/KS/Huddinge. If anyone have any good ideas, you are more than welcome to contact me with suggestions at ebba.brakenhielm@mtc.ki.se. It could for instance be in the form of a traditional conference with invited speakers, a big party or maybe some exciting day out in the field? The main purpose is that it should be a pleasurable event that as many as possible will want to take part in…

It seems that at last the **MTC pub** will come to life again! The brave hearts that have volunteered so far, the rumors have it, are PhD students of Dutch origin. We all thus can look forward with great anticipation to soon hear more about upcoming exciting events in the MTC main entrance hall…

More later**!**

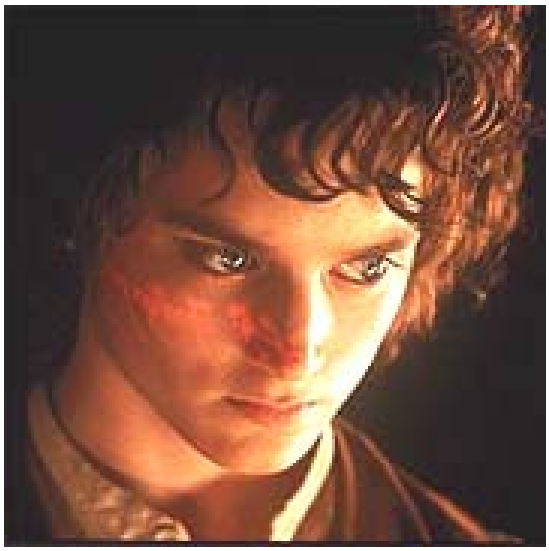
Ebba Bråkenhielm

STUDENT LIFE

The Lord of the Rings: an allegory of the PhD?

The story starts with Frodo: a young hobbit, quite bright, a bit dissatisfied with what he's learnt so far and with his mates back home who just want to get jobs and settle down and drink beer. He's also very much in awe of his tutor and mentor, the very senior Professor Gandalf, so when Gandalf suggests he take on a short project for him (carrying the Ring to Rivendell), he agrees. Frodo very quickly encounters the shadowy forces of fear and despair which will haunt the rest of his journey and leave permanent scars on his psyche, but he also makes some useful friends. In particular, he spends an evening down at the pub with Aragorn, who has been wandering the world for many years as Gandalf's postdoc and becomes Frodo's advisor when Gandalf isn't around. After Frodo has completed his first project, Gandalf (along with Head of Department Elrond) proposes that the work should be extended. He assembles a large research group, including visiting students Gimli and Legolas, the foreign postdoc Boromir ,and several of Frodo's own friends from his undergraduate days. Frodo agrees to tackle this

larger project, though he has mixed feelings about it. ("'I will take the Ring', he said, 'although I do not know why.'") Very rapidly, things go wrong. First, Gandalf disappears and has no more interaction with Frodo until everything is over. (Frodo assumes his supervisor is dead: in fact, he's simply found a more interesting topic and is working on that instead.) At his first international conference in Lorien, Frodo is cross-examined terrifyingly by Galadriel and betrayed by Boromir, who is anxious to take the credit for the work himself. Frodo cuts himself off from the rest of his team: from now on, he will only discuss his work with Sam, an old friend who doesn't really understand what it's all about, but in any case is prepared to give Frodo credit for being rather cleverer than he is.



Then he sets out towards Mordor. The last and darkest period of Frodo's journey clearly represents the writing-up stage, as he struggles towards Mount Doom (submission), finding his burden growing heavier and heavier yet more and more a part of himself; more and more terrified of failure; plagued by the figure of Gollum, the student who carried the Ring before him but never wrote up and still hangs around as a burnt-out, jealous shadow; talking less and less even to Sam. When he submits the Ring to the fire, it is in desperate confusion rather than with confidence, and for a while the world seems empty. Eventually it is over: the Ring is gone, everyone congratulates him, and for a few days he can convince himself that his troubles are over. But there is one more obstacle to overcome: months later, back in the Shire, he must confront the external examiner Saruman, an old enemy of Gandalf, who seeks to humiliate and destroy his rival's protegé. With the help of his friends and colleagues, Frodo passes through this ordeal, but discovers at the end that victory has no value left for him. While his friends return to settling down and finding jobs and starting families, Frodo remains in limbo; finally, along with Gandalf, Elrond and many others, he joins the brain drain across the Western ocean to the new land beyond.

Rutger van der Holst

News from AII

Money for student-initiated activities available!

Always have excellent ideas on activities that would improve your research education, but the boss always says no? Here's the solution! The research program in Allergy, Immunology and Inflammation (AII), that has its administrative base at MTC, launches a fund for student-initiated activities. SEK 100.000 is available yearly for activities conceived and arranged by students. The activities should ideally be of general interest and availability for all students within the areas covered by the program, but special activities for smaller student groups will also be considered. An application is needed in which the purpose of the activity is explained, accompanied by a description of the activity and the group of students involved. The steering board of AII will then decide whether or not the activity will be funded. Use your creativity and take this opportunity to influence your PhD education.

Read more about this on AII:s homepage which will be available within a few days at http://www.ki.se/edu/research/programmes/aii. There you can also find more information on the program including the PhD courses we administrate.

Supervisors – register your new students on our research preparatory course!

For one year now, AII has run a research preparatory A level course that helps to build bridges between preclinical and clinical activities as well as to facilitate recruitment of talented PhD students. During this 20 p course, each student conducts an extensive project within a preclinical research group that has an AII orientation. This work is complemented with two placements of a week each at two hospital clinics. The idea is for students to meet patients with diseases that are of relevance to their projects, attend different treatments and investigations and thus gain insights into clinical work and research. Possible clinics include those specializing in allergy, rheumatology, neurology or endocrinology, and the idea is to find a close match between the student's project and the clinical reality benefiting from it.

During the course, you are able to offer the student a stipend, and they are also eligible for student loans. Students and supervisors interested in the course are encouraged to together submit an application to the steering board of AII. Application form can be found on our homepage, or obtained from Louise.Berg@mtc.ki.se, to whom you should also send your application. Students are admitted to the course through decisions from the steering board. The steering board has two more meetings this spring, on March 19 and May 14. Application deadline is one week before the meeting. AII provide a bench fee of SEK 10.000 per student to the research group.

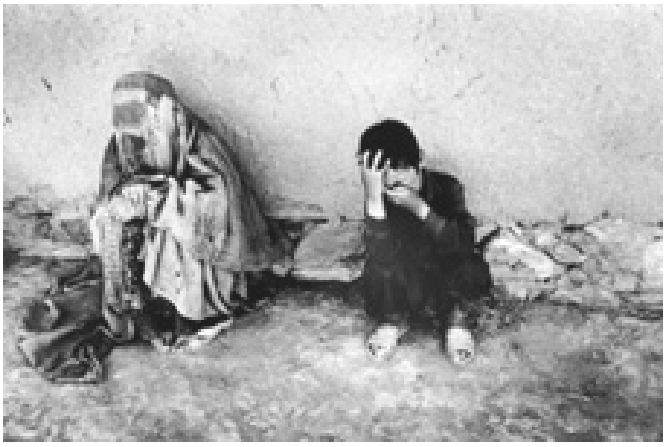
During the first year, this course has proven to be an excellent introductory period before registration for full PhD studies, both for the supervisor and for the student. Take this opportunity to try each other out, in a way that gives the students a taste of what preclinical medical research is all about in the end – helping and curing patients!

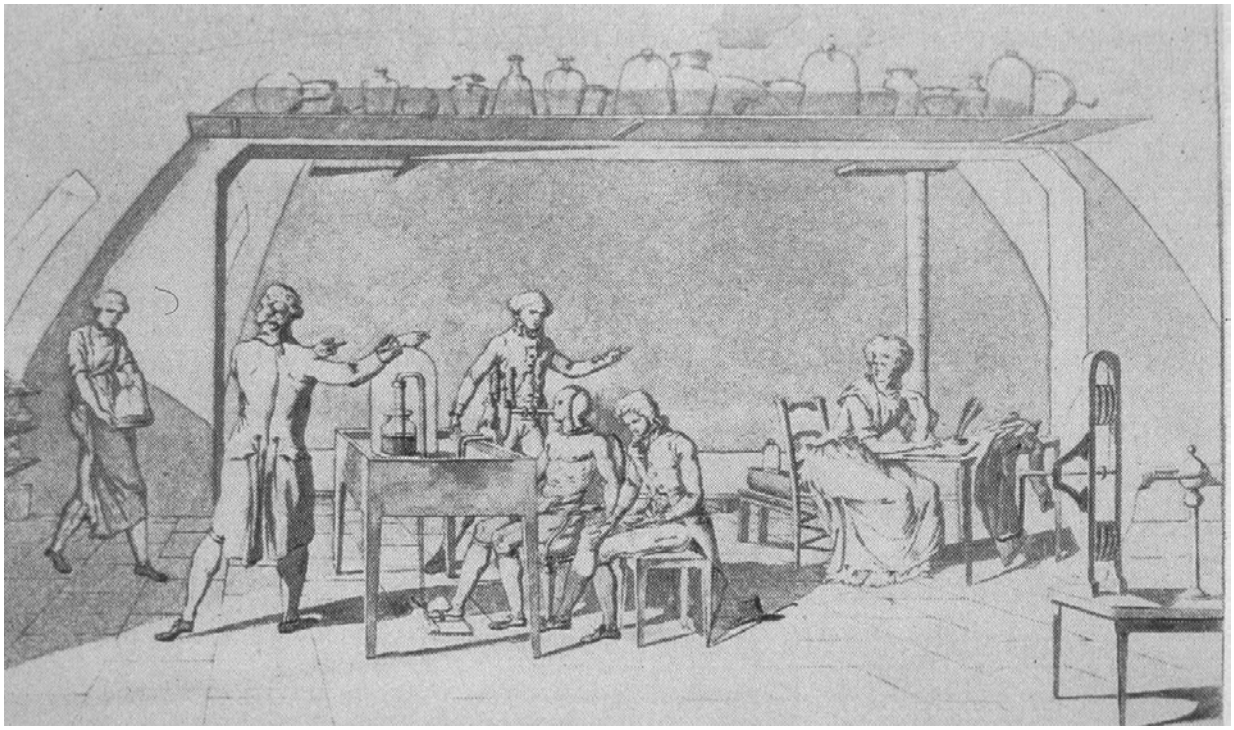
Petter Höglund
Chairman AII Steering Committee
728 62 01
petter.hoglund@mtc.ki.se

Rädda Barnen
Save the Children Sweden

We want to thank all contributors to our recollection of money for Rädda Barnen made at MTC. The final sum amounted to **3.125:50 SEK**!!! The money was sent to Afganistan in January we were told by Rädda Barnen. Thanks again!!!

Farideh Sabri





MME LAVOISIER

In 1771 Marie Anne Pierrette Paulze was a lively girl of 13. When her mother passed away, the young woman left a convent school to help her father as a hostess.

Antoine Laurent Lavoisier had a law degree, but his passion was for science. He impressed the French scientific establishment with his geological and chemical research. Lavoisier bought a half share in the *Ferme Générale* , a private company collecting taxes for the crown. Marie Anne's father was one of the directors.

Lavoisier was a frequent visitor at the Paulze house. He and Marie Anne played romantic board games, but also spoke of geology, chemistry and astronomy. When the father proposed a marriage, both welcomed it. Antoine was 28, Marie Anne 13.

Antoine Laurent Lavoisier

This young natural philosopher mastered the art of careful experimentation in chemistry and physics. Independently wealthy from his *fermier*'s income, he filled a private laboratory with balances, burning lenses and metal vessels of an unmatched magnitude and quality. In a way, Lavoisier's science was the big science of his day.

Lavoisier gave the first correct accounts of burning, respiration and rusting. In bringing about the Chemical Revolution, he properly defined the elements (though he thought heat was one), showed that water was a compound and air a mixture, and proposed a new systematic nomenclature for chemistry. In the remainder of his time, he dealt with numerous practical problems —he debunked mesmerism, thought about contagious disease in cities, ensured that young America got its gunpowder, adjudicated disputes on ballooning and, after the revolution, participated in the work on the metric system. Citizen Lavoisier's work for the French Republic did not save him from the Jacobin terror. On May 8, 1794, he and his father-in-law were executed, along with 26 others working in the Ferme Générale.

Her Husband's Helpmeet, and After

From early on in her marriage Mme. Lavoisier took instruction in chemistry to help her husband in his work. She learned to read English to translate books for Lavoisier. She learned to draw from Jacques-Louis David.

On a portrait (by David) Mme Lavoisier's arm rests on her husbands shoulder. But there is a distance between them. To me there is also a certain tension in her leaning posture. I imagine: is she pressing in, and would like to enter Lavoisier's realm of instruments in the right-hand part of the picture? Lavoisier looks at his wife—she looks out as us, at the world. They had no children.

After her husband's death, Mme. Lavoisier herself spent 65 days in jail. Emerging, she recovered his confiscated books and kept his works in print. In 1805 she married the American/British/Bavarian adventurer, inventor and scientist Benjamin Thompson, Count Rumford. The marriage was an unhappy one—it's reported that she poured boiling water on his flowers—and ended four years later. Mme. Lavoisier lived on until 1836.

There is no biography of Mme. Lavoisier. She figures importantly in "Oxygen," a play which I have written with Carl Djerassi (the creator of the Pill). "Oxygen" is about the discovery of the element to be sure, but more than that, the play is about the passion to be first, the problematic nature of discovery, and ethics. And about the Nobel prizes and the role of women in science, too. "Oxygen" has had American, British and German productions in 2001, but strangely enough (for a play set entirely in Stockholm) no Swedish performance.

But Was She a Chemist?

There is no published scientific paper in Marie Anne Lavoisier's name. With Mme. Picardet's help, she translated from the English Kirwan's "An Essay on Phlogiston," with notes by Lavoisier and friends, notes intended (correctly) to systematically demolish Kirwan's argument. The original edition did not carry her name as translator.

Elsewhere, she draws herself in their laboratory. Two of her strikingly realistic and beautifully composed images of Lavoisier's work on respiration survive. These are classic visual documents of chemical experimentation. In the picture here Mme. Lavoisier is sitting at a table, quill in hand. She turns to observe the experiment, waiting to write down the measurements as they are called out by her husband or his assistant. Here she is an amanuensis. She was more at times; she also wrote the plan for what experiments were done at Lavoisier's laboratory on a particular day.

And Marie Anne Lavoisier produced the plates for Lavoisier's *Traité Elémentaire de Chimie*, published in the year 1789, that of another Revolution. In Cornell's library are her watercolor sketches for the 13 remarkable plates that illustrated the book that changed chemistry. In the book there is no credit to her, only the plates are signed *Paulze Lavoisier sculpsit*, to testify to her engraving.

Mme. Lavoisier could not have been a chemist. No fault of her own, for she had the intelligence and the training—society did not allow women to follow that path for a hundred years after her time. That's how long France had to wait for another Marie.

There were exceptions, for in many ways 18th-century French culture did provide a place for women as intellectuals, more so than other European societies of the time. Forty years earlier we encounter the Marquise du Châtelet (1706-1749), who studied mathematics and physics. She married, in the normal way of aristocracy, and led an intellectual life separate from her marriage. Voltaire, her lover for some years, encouraged her to undertake the first full French translation of Newton's *Principia*. This she did, ably so, and also wrote about Leibniz's work. A younger contemporary of Mme. Lavoisier was the mathematician Sophie Germain (1776-1831), who used a pseudonym to come into professional contact with J. L. Lagrange and C. F. Gauss.

The exceptions were just that; the world of the Salons—an exciting intellectual world to be sure—and a correspondence with natural philosophers is what upper class women could aspire to. At best. I speculate that Mme. Lavoisier was not resentful; she shifted her creativity into other channels, as many a woman has done over millennia.

Still, when I think of the story of Mme. Lavoisier, I feel a great loss, a sadness. This smart woman was isolated from the scientific world. As her

drawings and the historical record testify, Mme. Lavoisier moved in the company of scientists, and good ones at that. The sadness that comes over me is that they, and her husband in the first line, did not recognize her abilities

Roald Hoffmann
Cornell University, Ithaka, NY

Contributed by *Eva Klein*

HOW IT WAS DISCOVERED

THE DISCOVERY OF EBNA

Continued from p 1

What kind of a virus is this? - Tony asked. Neither we nor a couple of colleagues on John's staff who were familiar with viral electron microscopy, could disagree with Tony's diagnosis. The particles resembled a herpes virus. The lymphoblastoid cells, derived from a BL line that harbored them did not look happy. They showed signs of degeneration or were already dead.

Tony told us that he has established a number of such lines from BL biopsies. Only some of them contained the virus-like particles. All of us, including Epstein, were of the opinion that Tony's cells have probably picked up a passenger virus, perhaps herpes simplex, from the presumably immunodefective human host.

In parting, Epstein declared that the virus could well be a wild goose, but it is a goose that has to be chased. Right he was.

The first indication that it was not a previously known goose came from the work of the prominent virologists, Gertrude and Werner Henle in Philadelphia. They used serological methods to examine some of the same BL lines that Epstein has studied. Their first important paper that became one of the classics of the field was rejected by several virological journals, because it was entirely based on immunofluorescence and described a very unorthodox virus. It was finally published in the Journal of Bacteriology (Henle, G., Henle, W. Immunofluorescence in cells derived from Burkitt´s lymphoma. J. Bact. 1966, 91: 1248-1256). The tests showed that the virus Epstein has seen in the electron microscope was not identical with any of the known herpesviruses (Epstein, M.A, Achong, B.G, Barr, Y. M., Zajac, B., Henle, G., Henle, W. Morphological and virological investigations on cultured Burkitt tumor lymphoblasts (strain Raji). J. Nat. Cancer Inst., 1966, 37: 547-559).

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Meanwhile, our efforts also started to bring fruit. Using the membrane immunofluorescence technique we have developed earlier to detect virally induced surface antigens on murine leukemia cells (Klein, G., Klein, E., Haughton, G. Variation of antigenic characteristics between different mouse lymphomas induced by the Moloney virus. J. Nat. Cancer Inst. 1966, 36: 607–621), we could detect a membrane antigen in some BL lines (Klein, G., Klein, E., Clifford, P. Search for host defenses in Burkitt lymphoma: Membrane immunofluorescence tests on biopsies and tissue culture lines. Cancer Res. 1967, 27: 2510-2520).

When I first met the Henles at a conference in Rye, New York, in 1967, we compared notes. Our membrane antigen was present on some of the same lines where Epstein had seen the virus and where the Henles detected what turned out to be the viral capsid antigen. The circle has been closed. Werner Henle and I decided to name the new virus, referred to as a "herpes-like virus" until this point, the Epstein-Barr virus (EBV).

My encounter with the Henles was the starting point for an intense collaboration that went on uninterruptedly for 22 years, until the death of Werner, and has resulted in 73 joint publications.

Using their serological test for the EBV-encoded viral capsid antigen (VCA), the Henles have conducted an extensive survey to establish the prevalence of EBV-antibodies in human populations. It turned out that the virus is ubiquitous. It showed no preference for the high endemic BL regions. No virus free niches could be found anywhere in the world. In the developed countries, antibody prevalence could be related to socioeconomic status, however. In the low socioeconomic groups most children became infected during their early years and 90% or more of all adults were seropositive. In high socioeconomic groups, only 10-20% of the young children became positive. A second rise in the frequency of EBV-seropositives occurred during the teens. Eventually, 80-90% of the adults became seropositive in this category as well.

The etiological connection between EBV and infectious mononucleosis was discovered in 1968 by a serendipitous observation in the Henle laboratory (Henle, G., Henle, W., Diehl, V.

Relation of Burkitt's tumor-associated herpes-type virus to infectious mononucleosis. Proc. Nat. Acad. Sci. 1968, 59:94-101). EBV seronegatives were in great demand by this time, since their serum and lymphocytes were used as controls in many studies. A laboratory technician who belonged to this precious minority developed mononucleosis. When she returned after convalescence, she was seropositive. Subsequent retrospective and later prospective studies confirmed that only EBV-seronegatives develop classical, heterophile positive mononucleosis and they all convert to seropositivity in the course of this process (Evans, A.S., Niederman, J.C., McCollum, R.W. Seroepidemiologic studies of infectious mononucleosis with EB virus. New Engl. J. Med., 1968, 279: 1121-1127). This meant that antibodies against EBV protected against the disease, indicating that EBV is the causative agent of mononucleosis. This was further corroborated by the detection of infectious virus in the saliva of mononucleosis patients that could transform normal B-cells into immortalized lymphoblastoid cell lines (LCLs).

It is interesting to note that the lay names for mononucleosis, coined long before EBV was discovered, college disease and kissing disease, made perfect sense. It was a college disease, because only youngsters from the hygienically protected groups that reached adolescence or became young adults without being infected with EBV got mononucleosis. Salivary transmission made it the kissing disease.

It is still an unsolved puzzle why small children do not develop mononucleosis after primary infection. They undergo "silent seroconversion" instead. The dominating early childhood infection protects the low socioeconomic groups from mononucleosis.

Interestingly, early childhood infection is also common in the people of the Far East, irrespectively of socioeconomic status. This has been attributed to the habit of chopstick use and the frequent picking of food from a common bowl. It guarantees early infection by salivary contamination and therefore protection from mononucleosis!

EBV transformation. The transforming, or, more appropriately, immortalizing effect of the virus was first discovered when irradiated BL cells that produced small amounts of virus were cocultivated with cord blood cells. EBV is not transmitted vertically and cord blood cells are therefore always virus negative. The same could be achieved by the addition of filtered virus containing culture fluids. Resting B-cells turned into proliferating immunoblasts. The derived continuously growing lymphoblastoid cell lines (LCLs) either did or did not release virus. Some of the non-producers could be induced to make virus by chemical compounds like butyrate, phorbol esters, bromo- or iododeoxyuridine or by anti-immunoglobulin antibodies. Other lines were non-inducible by these agents.

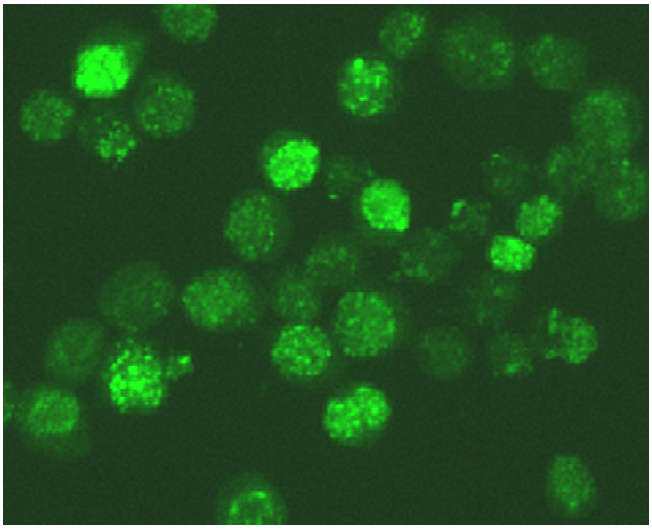
All this indicated that Epstein's demonstration of herpes-like virus particles in some BL lines, the Henles staining of VCA and our staining of viral envelope antigens in the same lines only detected the top of the iceberg. What was hidden under the surface?

The discovery of EBNA. In 1970, zur Hausen, the Henles and our group published a joint paper in Nature (zur Hausen, H., Schulte-Holthausen, H., Klein, G., Henle, W., Henle, G., Clifford, P., Santesson, L. EBV DNA in biopsies of Burkitt tumors and anaplastic carcinomas of the nasopharynx. Natue, 1970, 228: 1056-1058), describing the detection of EBV-DNA in tumor biopsies from BLs and nasopharyngeal carcinomas (NPC) by DNA/DNA hybridization. All 13 BL and all 10 NPC biopsies carried multiple viral genome copies per cell. Since in vivo tumors are non-virus producers, this indicated that they may carry the viral genomes in a repressed form. We suspected the same would hold true for the non-producer and non-inducible cell lines. But definite proof was lacking. We were wondering whether EBV-carrying cells would express a nuclear antigen, like cells transformed by the better known DNA tumor viruses, such as polyoma, SV40, and the adenoviruses. Conventional indirect fluorescence staining gave no clear results on the EBV-carring BL and LCL lines, however. We were therefore looking for a viral marker that would be detectable at the cell level in virus carrier but non-producer lines.

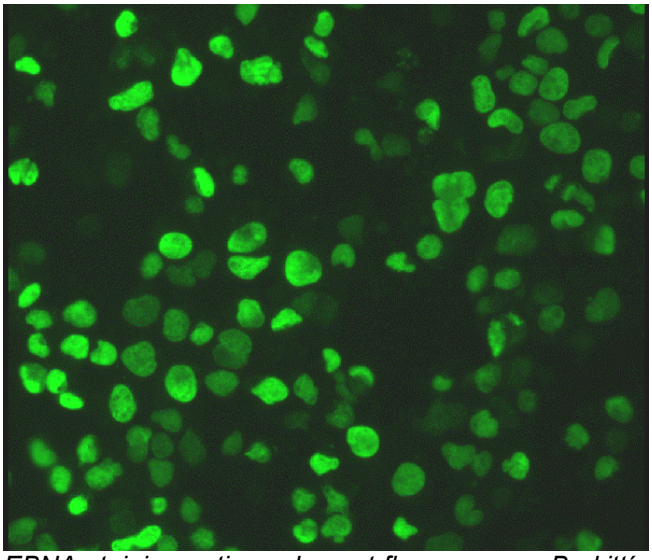
Our discovery of EBNA departed from an earlier finding of Armstrong and the Henles (Armstrong, D., Henle, G., Henle, W. Complement fixation tests with cell lines derived from Burkitt´s lymphoma and acute leukaemias. J. Bact., 1966, 91: 1257.1262). They detected a soluble, complement-fixing antigen in both virus producing and non-producing African BL derived lines. We remembered that weak indirect fluorescence reactions could be amplified by

adding a complement step after the antibody and staining the activated complement with an FITC-conjugated anti beta 1C (activated C3) reagent (Hinuma, Y., Ohta, R., Miyamoto, K., Ishida, N. Evaluation of the complement methods of fluorescent antibody technique with myxoviruses. J. Immunol., 1962, 89: 19-26). The amplification is due to the fact that only a fraction of the antigen combining antibodies gives a signal in indirect fluorescence where one labeled antibody molecule reacts with one antigen, but 300 complement (C3) molecules are bound to each antigen-antibody complex.

I asked my Australian postdoctoral fellow, Beverly Reedman, to try an anticomplement immunofluorescence reaction (ACIF) in our search for a nuclear antigen. Beverly made the test and lo and behold, the nuclear antigen appeared sparkling and brilliant in all its beauty



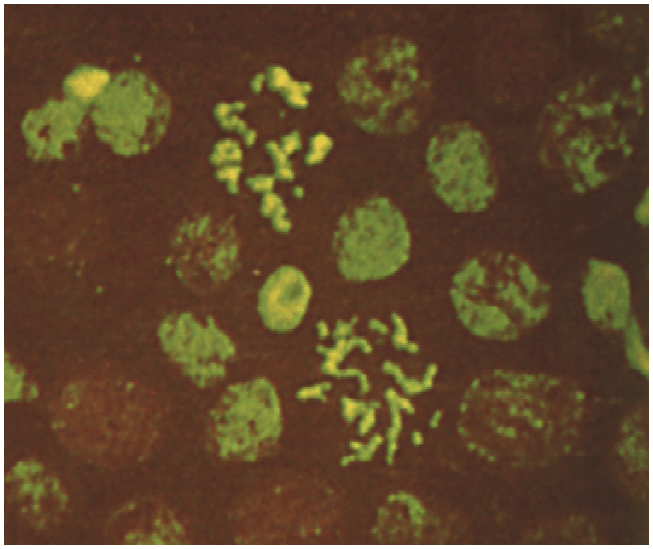
EBNA staining anticomplement fluorescence. Lymphoblastoid cell line. Courtesy of Laszlo Szekely



EBNA staining anticomplement fluorescence. Burkitt´s lymphoma line. Courtesy of Laszlo Szekely

It was present in virtually all cells in the EBV-DNA positive lines. We called it EBNA for EBV (determined) nuclear antigen (Reedman, BM., Klein, G. Cellular localization of an Epstein-Barr virus (EBV)-associated complement-fixing antigen in producer and non-producer lymphoblastoid cell lines. Int. Journal of Cancer, 1973, 11:499-520). It was also present in nearly 100% of the cells in all EBV-DNA positive biopsies including both BL and nasopharyngeal carcinoma (NPC). In contrast, EBV negative BL or other lines did not express EBNA.

Unlike the SV40 encoded large T antigen, EBNA was associated with the chromatin, not with the nuclear sap. In mitotic cells, whereas SV40 LT distributes diffusely throughout the cytoplasm, EBNA stayed in the metaphase chromosomes, without any specific localization



(EBNA stained metaphase chromosomes in BL line. From Reedman and Klein).

As far as NPC is concerned, the EBNA staining settled an important question that could not be decided earlier on the basis of nucleic acid hybridization. EBV-DNA could be detected regularly in anaplastic or low differentiated NPCs, irrespectively of their geographic and ethnic origin. However, the heavy lymphocytic infiltration, characteristic for the tumor, raised the question whether the viral genomes were carried by the lymphoid or the epithelial elements. The EBNA staining indicated that the virus was present in the carcinoma cells. This was further supported by our finding with Mikael Jondal, showing that the NPC-infiltrating lymphocytes were largely T-cells,not the readily EBV-infectable B-cells (Jondal, M., Klein, G. Classification of lymphocytes in nasopharyngeal carcinoma (NPC) biopsies. Biomedicine, 1975, 23:163-165). The final evidence came from our collaborative study with Beppino Giovanella (Klein, G., Giovanella, B.C., Lindahl, T., Fialkow, P.J., Singh, S., Stehlin, J.S. Direct evidence for the presence of Epstein-Barr virus DNA and nuclear antigen in malignant epithelial cells from patients with poorly differentiated carcinoma of the nasopharynx. Proc. Nat. Acad. Sci., 1974, 71:4737-4741). NPC biopsies received from Peter Clifford in Nairobi were shipped live from Stockholm to Texas, where Beppino transplanted them to nude mice. The implants grew into tumors that could be transplanted serially during a few passages. All human lymphocytes were lost already after the first passage. The tumors continued to show the histological pattern of anaplastic carcinoma. They remained EBNA positive. In fact, the average amount of EBV-DNA per cell increased during nude mouse passage, due to the loss of the EBV negative human lymphocytes.

Subsequently, the "EBNA test" became a standard method in all EBV laboratories. Further studies showed that "EBNA" was actually a family of 6 proteins (Klein, G., Giovanella, B.C., Lindahl, T., Fialkow, P.J., Singh, S., Stehlin, J.S. Direct evidence for the presence of Epstein-Barr virus DNA and nuclear antigen in malignant epithelial cells from patients with poorly differentiated carcinoma of the nasopharynx. Proc. Nat. Acad. Sci., 1974, 71:4737-4741), the function of which is still only partly known. A review of the six EBNAs is beyond the scope of this article.

Georg Klein

WEBMASTER'S VOICE

The MTC Chat Forum is dead. Due to a massive lack of interest this service has been terminated. If you by any chance have an idea about what else should be removed or possibly be included in the MTC website, please let me know.

Otherwise I just want to post a few links that could be useful for the newly appointed group leaders as well some of the already established ones when it comes to ***upload and update the group pages on the server.***

http://www.mtc.ki.se/misc/simple_rules.htm
http://www.mtc.ki.se/misc/template.htm
http://www.mtc.ki.se/misc/template_nav.htm

Per Hagblom
Per.Hagblom@mtc.ki.se

MTC Papers-of-the-Month

Proc Natl Acad Sci U S A 2002 Jan 22;

***Functional p53 chimeras containing the Epstein-Barr virus Gly-Ala repeat are protected from Mdm2- and HPV-E6-induced proteolysis*.**

Heessen S, Leonchiks A, Issaeva N, Sharipo A Selivanova G Masucci MG,Dantuma NP

Functional inactivation of the tumor suppressor protein p53 by accelerated ubiquitin/proteasome-dependent proteolysis is a common event in tumor progression. Proteasomal degradation is inhibited by the Gly-Ala repeat (GAr) of the Epstein-Barr virus nuclear antigen-1, which acts as a transferable element on a variety of proteasomal substrates. We demonstrate that p53 chimeras containing GAr domains of different lengths and positions within the protein are protected from proteolysis induced by the ubiquitin ligases murine double minute 2 and E6-associated protein but are still ubiquitinated and retain the capacity to interact with the S5a ubiquitin-binding subunit of the proteasome. The Gar chimeras transactivate p53 target genes, induce cell cycle arrest and apoptosis, and exhibit improved growth inhibitory activity in tumor cells with impaired endogenous p53 activity.

Mol Cell Biol 2002 Feb;22(4):1194-202

***Deletion of the laminin alpha4 chain leads to impaired microvessel maturation*.**

Thyboll J, Kortesmaa J, Cao R, Soininen R, Wang L, Iivanainen A, Sorokin L, Risling M, Cao Y, Tryggvason K.

The laminin alpha4 chain, a component of laminin-8 and -9, is expressed in basement membranes, such as those beneath endothelia, the perineurium of peripheral nerves, and around developing muscle fibers. Laminin alpha4-null mice presented with hemorrhages during the embryonic and neonatal period and had extensive bleeding and deterioration of microvessel growth in experimental angiogenesis, as well as mild locomotion defects. Histological examination of newborn mice revealed delayed deposition of type IV collagen and nidogen into capillary basement membranes, and electron microscopy showed discontinuities in the lamina densa. The results demonstrate a central role for the laminin alpha4 chain in microvessel growth and, in the absence of other laminin alpha chains, in the composition of endothelial basement membranes.

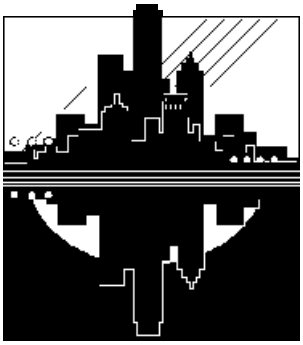
Science 2002 Jan 18, 295(5554)443-5

SCIENCE IN EUROPE:
Framework Programmes Evolve
Wigzell H

Europe is presently undergoing a most exciting period of transition. Via a cobweb of changes, a large number of nations are moving toward creating a federation of states, the European Union (EU). It is possible that in the end all of Europe, with Russia and Turkey, will be included. This is an experiment of a kind never tried before and it will be ongoing for many years. Strategic components for the success of this venture, such as research and innovation, will be dependent on well-understood, clearly organized structures with clear-cut organizations. The EU has chosen for the first decades of its existence to use a series of changing Framework Programmes to create what has been called a European Research Arena. Elements of these Framework programs aim to promote a European identity through such activities as supporting collaboration between scientists across national borders and encouraging movements of researchers between universities in different countries. A fundamental underlying principle has also been to link research with innovation, in a way that reduces the distance between basic research, applications, and products.

(For the whole text see reference above)

CREDIT: JOE SUTLIFF



General News

AWARDS

Georg Klein has been awarded the **Ingemar Hedenius Prize** and will receive it on the Day of Humanism on April 13th. The motivation of the Board is (in Swedish):

"Georg Klein tilldelas Ingemar Hedenius-priset år 2002, för att han rakryggat och konsekvent, under lång tid, har företrätt ett rationalistiskt och humanistiskt synsätt i livsåskådningsdebatten. Med sällsynt skärpa och djup har han förtjänstfullt bidragit till nyanserade analyser av frågor som gäller etik, filosofi och kultur.

Genom en rad böcker har Klein förmedlat viktiga erfarenheter och insikter både från sitt eget liv och från forskarvärlden, samtidigt som han har lyckats popularisera en vetenskaplig förståelse av den moderna biologin.

Georg Klein förvaltar också på ett utmärkt sätt traditionen från Ingemar Hedenius genom att som orädd och självständig debattör kunna kritisera religiösa och dogmatiska idéer på ett konstruktivt sätt. Hans insats bidrar därmed till att stimulera en förutsättningslös diskussion om centrala humanistiska värden och principer."

Hans Wigzell has been designated "**America's Swede of the Year**" by the Swedish Council of America and will receive the award on September 28th at a gala banquet in Seattle.

Hans G Boman has been awarded **Söderbergska priset** (800.000 SEK) from the Swedish Medical Association. This prize was given for his pioneering discoveries of "Anti-Bacterial Peptides". The prize will be handed over at a ceremony in April, in connection with a small symposium on anti-bacterial peptides organized by Hans himself.

SHORT NEWS

Mats Wahlgren has been appointed "Carl G. Harford Visiting Professor" at Washington University School of Medicine in St. Louis, USA.

TRANSLATIONAL RESEARCH PROJECT between MTC and SÖS

Bridging to applied science is of ultimate importance in future medicine. As hopefully most of you know MTC has built a translational research unit with Södersjukhuset, one of the biggest hospitals in Stockholm with a growing research interest.

Today we have created a new lab at the Research Center at SÖS and this is now in full activity. New groups have moved in there and we have got two PhD students registered and one post doc within the project. Another part of the work has been to invent new and ongoing projects at MTC–SÖS, and we have met the SÖS scientists both in large and smaller groups with a specific theme. This has resulted in new collaborations in which we hopefully will have synergy effects in a favorable way for the integration between modern biomedicine basic research (preclinical) and clinical research. MTC and SÖS have also got funding together for the organization of a course in preclinical-clinical integration for teachers that we will start soon.

At last, but not least I would like to congratulate **Eric Sandström** at Venhälsan, SÖS (coordinator), **Britta Wahren** and **Gunnel Biberfeld**. MTC/SMI who got funding for their research program about "DNA vaccination to HIV" from EU (1.1 million EURO).

Ewa Björling

NEWCOMERS AT MTC

There has been a nice production of babies in Francesca Chiodi's group:**Cara** was born in September, her mother is Liv Eidsmo. **Thea** also born in September, mother Catharina Missailidis. **Emil** was born in December, his mother is Anna Nilsson. The mothers and their babies turn up here now and then! Congratulations!

Anita Wallentin

MTC IN THE MEDIA

Yihai Cao was interviewed regarding his research on "reservatrol" in an article in **Svenska Dagbladet** on December 23. The article was entitled "Red wine cleans the coronary arteries" with the subtitle "Three glasses a day may deminish the risk of cancer". A very controversial point of view especially in Sweden! The same day **Expressen** had the headline "Why glögg saves your heart" on the same subject. Green tea is here mentioned as an non-alcoholic substitute.

Marie Bohm

APPLICATION TIME

For the February and soon the March application deadlines, please consult the MTC Inner Circle site: ***mtc.ki.se/intern*** You may also check the KI website: ***intra.ki.se*** by clicking on Forskningsfinansiering/ Funding

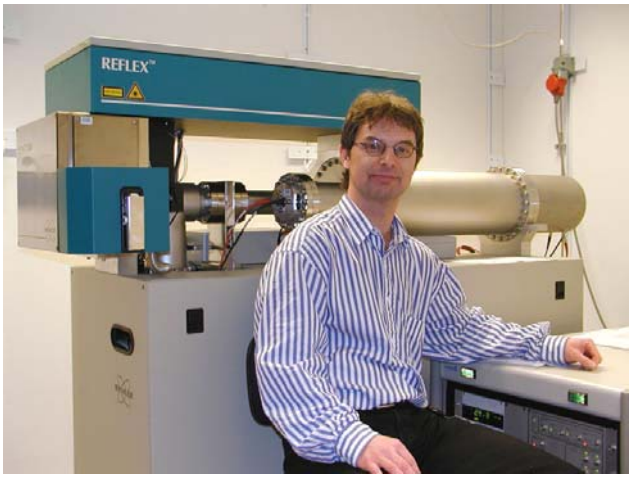
VI FINNER

Att de som är nöjda med tillvaron tycks finna förnöjelse I det enkla.
De klagar inte over världsläget eller över att de inte hinner med.

En morgontidning, en kopp kaffe och några vedpinnar I den öppna spisen är nog.

I det enkla uppstår inga krav!

Ur "Grunnaren I"
Av Gunnel & Kjell Swärd



MTC introduces a New Facility

A mass spectrometry has recently been installed at MTC, and we invite researchers to make use of it. The arrangement has been worked up by initiative of Prof.Emeritus Hans.G. Boman, and granted by The Knut and Alice Wallenberg Foundation and undersigned is responsible for the maintenance. Mass spectrometry comes in two flavors, one analyzing samples in solution (electrospray) and one where samples are co-crystallized with a matrix solution on a target plate (MALDI-TOF). Our machine utilizes the latter technique and allows the user to characterize peptides and proteins in proteome analysis. The facility is a shared one with SMI. In a near future it will be possible to process both individual samples as well as allowing more frequent users to acquire "driving licenses" in order to have better access to the facility. The mass spectrometry equipment is placed in the G-house, room G422 with workup stations being under set up in room F564 and at SMI.

There are probably many projects where you at MTC may find it practical to use mass analysis to solve a problem (see review by Larsen M.R., Fresenius J. Anal. Chem, 366, 677-690, 2000).

Check the MTC homepage under Scientific Core Facilities

Mats Andersson
728 6247

SEVEN NEW GRADUATE STUDENTS

Monica Hultcrantz "T-lymphocyte recognition of cells deficient in antigen processing" Supervisor: Elisabeth Wolpert

Juan Carlos Toro: "Improved assays for mycobacterial drug susceptibility studies, especially in Mycobacterium tuberculosis" Supervisor: Sven Hoffner

Jim Werngren: "The role of the Beijing family in multiresistant tuberculosis" Supervisor: Sven Hoffner

Michael Uhlin: "Regulation of early signaling events initiated upon engagement of T cell receptor (TCR) by the affinity of MHC:peptide/TCR interactions. Supervisor: Victor Levitsky.

Jenny Fernebro: "Bacterial programmed cell death and inflammation in pneumococcal disease". Supervisor: Birgitta Henriques-Normark.

Meit Björndahl: "The role of the VEGF family in physiological and pathological angiogenesis". Supervisor: Yihai Cao.

Ha Hoang: "Seroprevalence and serodiagnosis of Helicobacter pylori infection in Vietnam". Supervisor: Marta Granström.

CALL FOR CELL LINES TO THE MTC CELL COLLECTION

Hello all cell cultivators at MTC! I am responsible for building up a collection of Mycoplasma free cell lines at MTC. Would you like to contribute? I will test all incoming cell lines for occurrence of Mycoplasma before incorporating them into the collection (only if they are free of this insidious bug of course). The only thing you have to do is cultivate the cells for two passages in an antibiotic free medium and then give them to me.

The benefits of a common MTC cell collection are first that you will have a safe backup in case something would happen with your own storage of cell lines, second that you will get your cell lines Mycoplasma tested for free, and third that you and your dear colleagues at MTC will have cheap access to cell lines that you might otherwise have to pay a lot for.

Please contact me (Britt.Samuelsson@mtc.ki.se) so that we can discuss: 1) what cell lines you would like to contribute 2) when your cell lines will be available, and we will decide when the Mycoplasma testing should be done. SVARA GÄRNA PÅ SVENSKA OM MÖJLIGT.

Britt Samuelsson
Ext 6231

PE

STEM CELLS AND THERAPEUTIC CLONING

Report from my visit at the European Parliament in Brussels, December 2001

Background

What are stem cells?

Stem cells are cells that can divide to produce either cells like themselves (self-renewal), or cells of one or several specific differentiated types. Stem cells are not yet fully differentiated and therefore can reconstitute one or several types of tissues.

How does stem cell therapy work?

The aim of stem cell therapy is to develop differentiated cells or tissue for transplantation into patient suffering from diseases like diabetes, Alzheimer's disease, Parkinson's disease, stroke, chronic heart failure, etc. diseases for which we today have no efficient therapy or cure. Human stem

cells, appropriately reprogrammed, might be transplanted into tissue or organs, allowing constant regeneration.

What are the possible sources for stem cells?
One source for human embryonic stem cells would be to use 'spare embryos' - embryos that are no longer needed for infertility treatment. Another possibility would be to isolate embryonic stem cells from embryos created for research purpose or embryos created by somatic nuclear transfer (therapeutic cloning). These later stem cells would have the advantage of being immunologically compatible with the patient. **Foetal stem cells** can be derived from aborted foetuses and umbilical cord blood taken at the time of birth. **Adult stem cells** have been isolated from certain tissues such as bone marrow, skin and blood used for transplantation.

What are the ethical issues?
This promising area of research, however, raises controversy and ethical questions, focusing in particular on the method for obtaining stem cells. Furthermore, these innovative technologies may have profound human consequences that challenge our interpretation of universal ethical standards concerning human dignity and rights, the principle of freedom of research, the status of the human embryo, etc.

While ethical issues such as the status of the embryo, tissue banking and the use of genetic information have been addressed, other vital issues raised by stem cells research require attention. One issue that has received scarce bio-ethical attention to date is the possibility that stem cell therapies would extend human life expectancy considerably. Issues of population policy and global justice equally need to be addressed.

The European Commission
On 13 and 14 September 2001, the European Commission's Research DG gathered the co-ordinators of the 15 transnational R&D projects on stem cell therapy. The meeting made clear that the over one hundred participating laboratories work on stem cells taken only from adults, from umbilical cord blood or from aborted foetuses.

EU Commissioner for research, Philippe Busquin, said: "Stem cell research is among the proposed research priorities under the next Framework Programme for research (2002 - 2006). Stem cell-based therapies hold great potential for curing diseases and injuries. I believe we can gain a lot from a stronger exchange of information and co-ordination of stem cell research across Europe. But I want to make clear that European research programmes do not, and will not, fund research on embryonic stem cells that involves the creation of an embryo for research purposes."

The so-called **therapeutic cloning** is today excluded from EU R&D programmes in line with the recent opinion of the European Group of Ethics which said that this technology is still too immature and presents possible risks, despite its great potential.

The research project co-ordinators, together with the legal, ethics and industry experts who joined the meeting, concluded that it is an urgent need to know much more about stem cells before we can predict with confidence the future outcome of this kind of novel therapy. Europe needs a common policy and criteria for quality and safety assessment and evaluation of the efficiency of clinical trials.

In the end of November the European parliament rejected (after a heated debate) the recommendations of the report they had commissioned on the ethical, legal, economic and social implications of human genetics. While individual Member States are themselves responsible for decisions in this policy area, a European ban on human embryo experiments could nevertheless influence the future shape of EU funding. The decision taken on 29 November now means that a lot of funding be channelled into stem cell research - an outcome that is warmly welcomed by scientists pursuing research into therapeutic cloning, but a disappointment for those who completely oppose work on human embryos. The report resulted from a special parliamentary committee set up on human genetics that consulted scientists on both sides of the debate over an 11 month period. Had it been adopted in its original form it could have hindered EU plans to invest €2.15 billion over the next five years in health-related genetic research within the Sixth Framework Programme. Speaking on behalf of the European Commission, Research Commissioner Philippe Busquin, pointed out that the latest developments in this area underlined the urgent need for a balanced approach to genetic research taking account of ethical considerations.

Next step for the European Commission was to organise a conference on stem cell research in December 2001. This conference was entitled 'Stem cells: therapies for the future?'. The goal was to encourage a multidisciplinary and informative debate between scientists who were concerned with feasibility and consequences, and a wide range of representatives of society - experts in the ethical implications of biotechnology, specialists in human sciences and law, patients' associations, interest groups, students and teachers, educators and media, the medical profession, and various public authority representatives.
From this conference it could be concluded that:

- -The current research on human stem cells, either from differentiated tissue or from embryos, is scientifically sound and medically promising and should be actively developed and supported. Although the use of human stem cells in regenerative medicine is still at an early stage of development, it has the potential to deliver real progress in the treatment of various severe diseases

- The EU should continue to support research with all sources of human stem cells, including human embryonic stem cells.

- Reproductive cloning should be prohibited.

- Derivation of human embryonic stem cells from nuclear transplants (so-called therapeutic cloning) has not been achieved and appears to raise considerable difficulties. Research into additional strategies to overcome immune rejection is therefore to be strongly encouraged.

- Although the special moral status of the human embryo even prior to implantation should be respected, the conference consensus agreed on the use of spare human embryos for the preparation of embryonic stem cell lines. Research on human embryonic stem cells should be carefully regulated, peer reviewed, scientifically sound, directed towards substantial goals and ethically controlled.

- Publicly and privately funded research should be subject to the same regulations.

- A European registry of human embryonic stem cell lines should be established.

In summary, the Group considered that research on human stem cells offers valuable venues into developmental biology and medicine that could revolutionise therapy perhaps on a scale comparable to the introduction of antibiotics.

Ewa Björling

***Comment**: The European Life Sciences Group was set up in April 2000 by the Research Commissioner Philippe Busquin to meet his need for high level advice on life sciences and biotechnologies. One of the Group's tasks is to inform the Research Commissioner on the current situation in these fields and on imminent or foreseeable developments. Another duty is to contribute to the organisation and animation of a Life Sciences discussion platform, enabling scientists to engage in debate with the various "stakeholders" interested in the beneficial application and dissemination of the new knowledge.*

SUGGESTIONS FOR READING

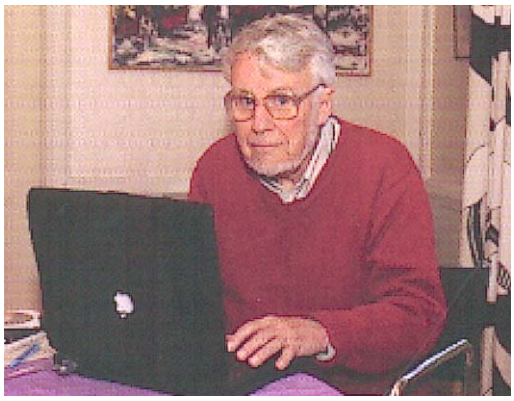
Hans G Boman's new memoir book is a "MUST" for every young scientist

("En egensinnig biologs liv skildrat av honom själv"; 208 pages, Anahit, Stockholm 2002; KI Medical Book shop: 185 SEK).

Hans G Boman has been awarded Söderbergska priset (800.000 SEK) from the Swedish Medical Association. This price was given for his pioneering discoveries of "Anti-Bacterial Peptides". The price will be handed over on a ceremony in April, in connection with a small symposium on anti-bacterial peptides organized by Hans.

Very timely he has also published his "memoirs" on how this discovery started 30 years ago. But it also an entertaining book on his experience of free university studies in 50ies, selecting research problems, research environments, building new departments and research teams, handling conflicts mixed with some popular introductions into his own research field and accounts of his broad interests in literature, art and society. I read it and found it so entertaining and "useful" that I decided to "edit & print" the book for Hans after it had been refused by Bonniers (also Astrid Lindgren was refused by them originally!). I can recommend the book to you. I think it is a MUST for young researchers. The name is "En egensinnig biologs liv skildrat av honom själv" (cp. Benvenuto Cellini; 208 pages, Anahit, Stockholm 2002). You can buy it in the KI Medical Book Shop (entrance Berzelius lab at the bus stop) for 185 SEK. We hope it will soon be available also at Akademibokhandeln. As the book was published in Swedish I here take the liberty to quote some words in Swedish from the Preface and from two short sections of the book on Creativity and on What it is about.

Ingemar Ernberg



Några omdömen om "En egensinnig biologs liv skildrat av honom själv":

Ur förordet : "Han (Boman) beskriver sina erfarenheter av att skapa framgångsrika forskningsmiljöer (i Umeå och på Stockholms Universitet) och väjer heller inte för det svåraste I forskaryrket, att välja problem, att bygga team och att hantera konflikter. Genom detta blir boken en värdefull erfarenhetskälla för framtida akademiskt ledarskap och för yngre forskare och doktorander. Genom sin ambition att även ge korta forskningsöversikter av popular natur, samt förmedla sina källor till inspiration och avkoppling har det blivit en underhållande resa genom "de två kulturerna" som vänder sig till en bred läsekrets"

Professor A (äldre): "... vissa delar enligt min uppfattning sådana att de skämmer boken och inte är värda att trycka".

Docent B (yngre): "Jag tycker det är en lättläst och rolig bok. Det är ju såhär det går till än idag. Och kastar man en sten i hopen skriker ju den som blir träffad."

Direktör C: "Jag skrattade högt när jag läste om befordringsärenden. Själv är jag välbekant med vågorna efter "vår kulturrevolution".

Redaktör D: "Den här minnesboken avslöjar hur det har gått till i vår universitetsvärd, men den når ingalunda till Lars Gyllenstens höjder."

Två små korta utdrag:

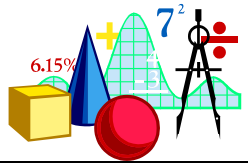
Från Kreativietsavsnittet:
"Vad är kreativitet och varför är det av intresse? - Kreativitet är en kapacitet för problemlösning, en hjärnans förmåga att kunna producera nya oväntade lösningar som kan variera från en bra

replik i en vanlig dialog till lösningen av ett mycket komplicerat vetenskapligt problem. Kreativitet är av intresse därför att egenskapen belönas på olika sätt. För det första är samhället angeläget om kreativitet och har därför tillskapat lockande yttre belöningar: Jobben som ger pengar, makt och prestige. För det andra finnes det starka inre belöningar: Att behärska ett yrke som kräver en komplex teknologi, organisationsförmåga och ögonblick av kreativitet skapar i sig tillfällen till en intensiv lyckoupplevelse."

Från Godtyckliga spår...
"Mitt främsta mål har varit att beskriva forskaryrket, på ett intellektuellt hederligt sätt, dvs. så gott det nu går. Det finns I boken ungefär där det historiskt passar in några populärvetenskaplig sammanfattningar, därav en om min senare forskning "Varför kan vi vara friska?" Men eftersom jag alltid läst rätt mycket, berättar jag i min näst sista del om fyra författare och fyra av deras böcker. Många biografier som jag läst skildrar möten med rader av berömda personer och samtal med stora andar som delat intressen som medeltida musik för blockflöjt eller Wittgensteins filosofi. Jag har inget sådant att bjuda på. Det jag vill skildra är arbetslivets vardag med framgångar (ibland) och rena misslyckanden."

Have you forgotten who is giving a ***seminar*** *today? Check the* ***new MTC Inner Circle*** *site and see MTC This Week on* ***www.ki.se/MTC/intern***

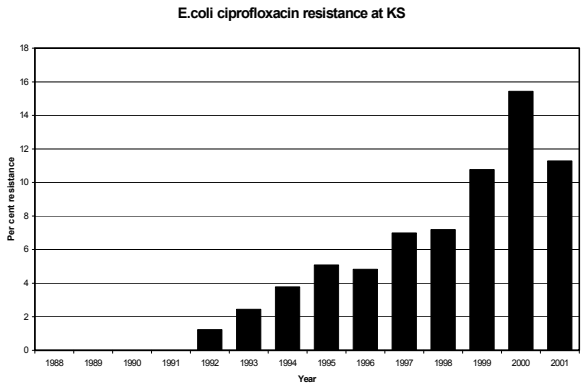
You will find a lot of other interesting and helpful information for MTCers there, blanks, mailing lists, application deadlines, common equipment, short news etc. Check it out and you will certainly find it very useful!



Research-Group-of-the-Month

THE GÖRAN KRONVALL GROUP[1]

Receptins are defined as binding structures in microorganisms that carry specific affinity sites for defined mammalian proteins[2]. Protein A of *S.aureus* and protein G of group G streptococci are well known examples. With **Måns Ullberg** previously in the group (now in Uppsala) we described plasminogen/plasmin receptins in several human pathogens, *Neisseria meningitidis, N.gonorrhoeae*, *S.pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and group A, C, and G streptococci. **Thomas Eberhard** showed that the plasminogen/plasmin receptin on pneumococci facilitated the penetration of reconstituted basement membrane by its capacity to protect the active, bound plasmin from inhibitors.



Klas Jönsson[3], PhD and inline virtuoso, has now added a new technique in the laboratory for receptin studies, phage display for cloning of procaryotic proteins with binding affinities. He has identified a protein in *Helicobacter pylori* with interesting biological activities. No function has previously been ascribed to this gene product.

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[1] http://www.ki.se/labmed/clim/gkgrp01.htm

[2] http://www.ki.se/labmed/clim/receptpd.htm

[3] http://www.ki.se/labmed/clim/gkgrp11.htm

A protein-deficient strain showed markedly lowered virulence in mouse model experiments performed in collaboration with **Betty Guo**, postdoc in Prof **John Mekalanos** laboratory at Harvard Medical School. Reconstitution of protein expression restored full virulence.

Together with **Hans-Peter Müller**, Lund, and **Hans-Jürg Monstein**, Linköping, this protein is now further characterized using BiaCore studies of recombinant proteins and mRNA analysis of clinical isolates.

Andreas Berge[4], PhD and infectious disease doctor, is pursuing his long-time studies of streptococci by collecting invasive isolates of group A strains together with non-invasive counterparts in our laboratory. His earlier studies on insertion sequences have led him to predict a role of these factors in the regulation of virulence factors.

The receptin studies are continuing, but another research area has also come into focus more and more, namely antibiotics and antibiotic resistance. Dr. **Mikael Sörberg**[5], PhD and infectious disease specialist, utilized our on-line database in clinical microbiology and performed a retrospective investigation of antibiotic resistance at Karolinska hospital during the years 1988–1999. Among all the information gathered, there were some alarming trends. Resistance to quinolones (for example norfloxacin and ciprofloxacin) showed a steady increase from zero to more than ten per cent.

Ciprofloxacin resistance among *E.coli* isolates at KS during 1988–2000.

The analysis of the data was performed by **Mikael Sörberg** together with our PhD student **Anna Farra**. She also extended the analysis to include a total of twelve laboratories in Sweden, representing most parts of the country, from Malmö to Falun. The trends were the same also in these hospital settings. Interestingly, extrapolation of the trends showed that the rise in resistance started at about the same time in the whole country, around 1990-1991. The consumption of quinolones showed a parallel increase during these years, but preceeding the resistance by some 5 years.

The molecular background for quinolone resistance in *E.coli* and other *Enterobacteriaceae* has been investigated by **Faiz Fendukly**, ST-Doctor in clinical microbiology. The classical mutations in topoisomerase II and IV genes were detected and a new mutation was also discovered. The sequences of the *Proteus mirabilis* gyrase genes were determined for the first time. The contribution of efflux pumps has also been investigated by **Faiz Fendukly** in collaboration with **Owe Källman**, ST-doctor in clinical microbiology and infectious diseases.

Faiz Fendukly, ST-Doctor in clinical microbiology at KS.

Another striking trend in the analysis, both at KS and in the country, was a continued rise in trimethoprim resistance in spite of the fact that the consumption of this drug had shown a decrease. A 20p-student from Uppsala, **Malin Grape**, now a graduated pharmacist, studied the possibility that this continued rise in resistance could be due to other resistance genes genetically linked to trimethoprim resistance. She looked for integrons in 105 clinical isolates of *E.coli* selected for trimethoprim resistance or multiresistance. She found 56 integrons in 50 strains. 46 of the integrons were of class 1. Amplified products from these 46 strains showed heterogeneity in molecular sizes. Fourteen products were sequenced from strains where the size didn't match resistance phenotype. In no case was there a gene cassett that could explain selection other than by a direct effect on the trimethoprim resistance genes (*dfr*). We also found a new type of *dfr*2 gene that was designated *dfr*2d.

[4] http://www.ki.se/labmed/clim/andberg1.htm

[5] http://www.ki.se/labmed/clim/mikkes01.htm

Project students Magnus Jöud, Malin Grape, Fataneh Jalili, and Martin Larsson have just finished their reports.

Another project student, **Fataneh Jalili** (20p project, Uppsala) has studied isolates of *E.coli* and *K.pneumoniae* from normal, healthy children in Vietnam regarding resistance phenotype and integron occurrence. Several new leads showed up in this as well as in the studies by **Malin Grape**. Also the 5p projects performed by **Magnus Jöud** and **Martin Larsson** on efflux pumps in Enterobacteriaceae and calculation of MIC values for strains using the M-test, respectively, gave new insight into these areas.

As was quite clear from the project performed by **Fataneh Jalili** as well as by our previous investigations in Vietnam performed by **Mattias Larsson**, there are great problems also in other parts of the world. This comes as no surprise. Together with **Mattias Larsson**, medical student and PhD student, and his head **Torkel Falkenberg**, docent at IHCAR, we are expanding antibiotic studies abroad in a EU project called ANTRES in collaboration with Professor **Alessandro Bartoloni**, Florenz, and Professor **Gian M Rossolini**, Siena, Italy, to Bolivia and Peru, a 10 million SEK project. These studies include antibiotic consumption and resistance as well as interventions. The results will increase the current understanding of antimicrobial use and resistance epidemiology in low-income countries and contribute to evidence-based policy making both nationally and internationally.

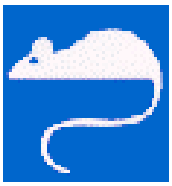
Query: ”***What is the most important test performed in the clinical bacteriology laboratory?***”
Answer: ”***The disk diffusion antibiotic susceptibility test***!”.

Query: ”***How could such a simple test be of any interest in research?***”

Well, on closer scrutiny we have found it a most powerful test and our studies have combined aspects on mathematics and biology in a fascinating way. We have defined an equation (SRA) which enables us to calculate regression lines (MIC values versus inhibition zone diameters) using only one single reference strain for each bacterial species, providing the means for a true calibration of the test. We have also designed a simple test for MIC determinations using a series of disks, the so called M-test. Finally, we have discovered a way to reconstruct the susceptible population of strains in a histogram of clinical isolates regardless of the number of resistant isolates also present. This might provide a way of making susceptibility tests from around the world comparable for surveillance purposes. So, we do have fun also with this simple method.

Göran Kronvall[6]

Klas Jönsson, Inga Karlsson, Anna Farra, and Göran Kronvall http://www.ki.se/labmed/clim/gkgrp01.htm



ANIMAL HOUSE NEWS

Animal log – försöksdjursjournal – for all experiments!

As you may have noticed, we recently had an inspection in the animal house from the local authorities. They come regularly to check our facilities and routines, in particular how well we comply with rules such as certificates (tillstånd), ethical permissions and trackable logs over all experiments. We passed the inspection quite well which made me happy. However, the delegation expressed concerns over our animal logs. According to the law, a written history (försöksdjursjournal) for each group of rodents that is being used for experiments must be kept in the animal house throughout the experiment and for several years after. For experiments being performed by the staff, this has been a working system for a long time. Our system to keep track on experiments performed by the researchers themselves at MTC has built on the idea that each scientist keeps his/her own detailed records of the experiments in the lab book, or perhaps on a separate sheet in a private location at the animal house. Unfortunately, this is not sufficient to fully comply with the law. Each group of animals in experiments must be followed on a log that is kept openly in the animal house. For each experiment there must be, at any time, a possibility for the staff, an inspector or anyone from the public, to get full information on the experiments that are being performed. This is important also if animals get sick, in which case instant information as to the type of the nature of the experiment must be available.

Taking advantage of the increased awareness of these rules that the inspection created, we will adopt this system from now on. This means that each one of you initially will have to adjust to a new routine requiring a bit more paper work. However, I trust that within a few weeks these routines will be seen as standard. I want to remind you about when we introduced the animal order form to get mice. This was then considered a heavy piece of extra work but is now a standard procedure that no one objects to. I hope that filling in an understandable animal log will soon be seen as an equally normal routine. Please consult Margareta Hagelin or anyone else in the staff to discuss how to write your log. The form for animal log that we have now is not perfect. We are working on an improved form for animal logs at the moment. In a couple of weeks, the staff and the animal house will dedicate a full seminar day to improving routines for this and similar matters. We will then present a new form but until now, please use the old one.

Animal order forms

I want to remind you about our new routines for using the animal order form. We are required by law to report each year how many mice we use at MTC. We have no problems recording the number of mice used from the breeding unit but have great problems with mice from the breeding we do not control, i.e. for which you as users pay cage costs and use freely. The system with writing on the door when you take mice has not worked. From now on we will test a system where you fill in an animal order form also for your own mice, i.e. a similar procedure as the one you use when you order MTC mice by fax. We hope that a uniform system for all types of mice will give us better control. You find plenty of copies of animal order forms in the corridor in the research unit. Fill it out and leave it in the research unit after you have finished your work.

Ethical applications

Please make sure that your experiment is supported by an ethical application. As you know, the number of your ethical application should be written on all your experimental cages. Remember that these include ALL cages with mice that have been manipulated – including those from which you have only taken a piece of tail or drawn blood. Weaned mice waiting for typing or experiments need not be marked.

Infection experiments

For those of you doing infection experiments, there is now a file with information on each pathogen as well as safety measures and precautions available. A colour code tells you

which type of sticker to put on your cage. With this system, the staff and your co-workers will know immediately which organisms are in the cage. Please make sure you label all your cages with the correct label.

BSL-III in "virorisken"

As you may remember, we have been working for some time to get BSL-III work with *M. tuberculosis* going in the viral risk unit. We will soon have an inspection from Arbetsmiljöverket but it has been slightly delayed. When cleaning up we discovered a water leak that had destroyed parts of the floor. It has now been dried up and after the technical investigation is finished we will hopefully be able to launch this exciting project (with an official inauguration ceremony!) and start the work.

Space

We have constantly been short of space in the reception unit. This is due to many incoming strains, but also to the fact that some incoming mice get stuck in the reception unit because they are not clean enough. During treatment, they take up space. Some immunodeficient mice are also kept in the reception unit because they need ventilated cages. We are improving the situation by buying new systems for ventilated cages. Last week, 60 cages in three new ventilated racks were installed. We also recently got 40 new cages from "virorisken" when it was emptied. This should improve the situation. There is also a more extensive plan on how to reshape the reception unit for which we have requested funding from KI. The request is currently being evaluated and we hope for a positive answer.

This will be all from now. Thank you all for helping us improving our routines! Don't forget that you can always call me or stop by C452 if you have things to discuss.

Petter Höglund
Tel: 728 62 01, Rm C452

MTC SPORTS CLUB

Hi everybody!
Soon the sun will be shining again and you will feel like running I hope. We are planning to participate in some relays and individual running competitions, such as "Vårruset", "Blod-omloppet" and "Dagbladsstafetten". If you are interested in joining the team, please send me an email: mia.lowbeer@mtc.ki.se, and also look for messages on the boards when we will have meetings to plan this.

I was really thinking of organizing a "Sports Sunday" this winter at Hellasgården, but again the snow melted away. But I will try, if we get some cold weather, again, either we can skate or ski or just play around in the snow. Keep your eyes open for messages. I guess we need to act quickly.

If that doesn't work I will try to organize a hike at "Sörmlandsleden" in May. Sörmlandsleden is a very long track, from Björkhagen in Stockholm to Nyköping in Sörmland. Each leg of the track is about 10-15km and there are several near Stockholm that you can reach by bus. I will come back with a date for this.
Keep on running!

Mia Löwbeer
C357, ext 6203, 6772

MY FAVORITE HOBBY

We here initiate a new series of articles on the interesting activities MTCers dedicate their spare(?) time to. Please share with us your great passions outside MTC! Malin Weiland, a dedicated multisporter, is the first one to go:

Adventure Racing – more than just an extreme sport

Hello all MTCers, yes it's me that you sometimes see running around in training clothes, who sometimes have my mountain bike by the stairs at level one and so forth. Marie has asked me to come forward by starting up this new series about things people, here at work, do at their spare time. As some of you already have realized I mostly spend my time in the forest out running or at the gym. I'm still one of those persons that seem to have too much energy and therefore need to spend it, and then I didn't have pipetting in mind (sorry Staffan).

I compete in something called Adventure racing (multisport in Swedish). During the races you combine mountain biking, running, canoeing, kayaking as well as climbing. You do it for several days in a row often without sleeping and all you know before you start is what you see on the map. The way the organizers check that you have gone through the whole course is by putting up checkpoints that you have to pass, just like orienteering. When people first hear about this they usually shake their heads thinking, how on earth can someone do that voluntarily they must be crazy. Well for starters most people into adventure racing, including me have an academic degree, are highly social beings and also like other normal things like partying. There is only one thing popping up in my mind that might be different for a racer - the willing to become physically exhausted. If you like that and enjoy getting adrenalin kicks you ought to get into this business. The picture above is from a competition we did last year from the Polar circle and down to Boden. In this particular spot we repelled down from the bridge into the boat and once at shore ran up to a military fortress called "Rödbersgsfortet" were we after 300 km crossed the finish line, exhausted but immensely happy.

There are also other sorts of races like mountain marathons that people, as well as I, tend to include in adventure racing. The picture below is from a competition called Fjällräven extreme marathon (FEM) that took place in Björkliden. In this competition you run 70 km up and down through hills in two days with tent, sleeping bags and food on your back.

I think most people enjoy the feeling of having accomplished something they were not sure they could manage. Maybe that's still why I keep on competing to get to know my own limits.

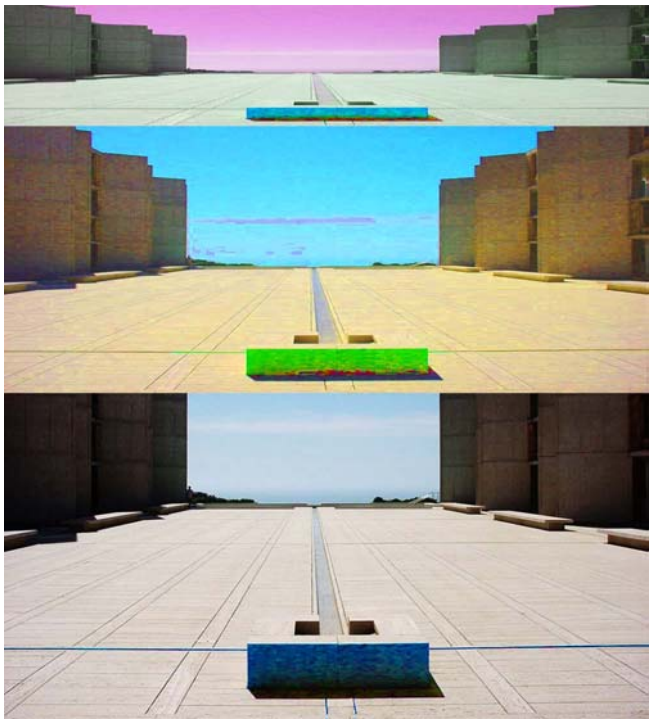
If I by now have not yet managed to talk you into this sport at least check out how my team is doing this summer and read stories about races we participate in at http://www.tengai.com/teamtengai.
See you around

Malin Weiland at the Parasitology unit.

MIXED FEELINGS AND THOUGHTS AT A DRIED OUT MICROSCOPE SLIDE

Marie thought that it's a great idea to have people dig in their drawers to find e g. microscopy pictures of some unexpected, visually attractive object. I've done the digging, but – where are they? I know they exist. I am contemplating on this evidence of black holes when sitting at the microscope in the dark. My mood changes as I see those actin filaments - bright red in the amoebas - smiling at a remark by Astrid (Fagraeus) "… if the authorities knew how fun it is to look in the fluorescence microscope they would impose a heavy entertainment tax on us!"

But what the h…! How stupid of me to mount these cells with culture medium instead of buffered glycerin. Now they are all drying up and the fluorescent staining gone –S..t! Even the cells are gone as the Dulbecco medium is all crystals. I see them growing. I mean, not the cells, the crystals! Why Dulbecco? Why didn't I use glycerin? I met him once, Dulbecco. It was a sunny day (of course) in 1971 before he moved to the Imperial Cancer Research Fund Laboratories in London. My boss Tom (Edgington) - whom I cannot congratulate these days in La Jolla as my eye doctor says no to flying due to my retinal bleeding last week – S..t! - phoned Salk and said: Hi Renato !… do you have some HepG2 cells around for my post doc… he will be over! So I met Dulbecco, this kind man who gave me the cells. (He was going to share the Nobel Prize 1975 with David Baltimore and Howard Temin for their work on the interaction between tumor viruses and nucleic acids of the host cells.) And nice to see the Salk Institute from the inside, framing the Pacific, water pouring along this narrow ditch, approaching the sea, a small waterfall, the sound of water! (See this fantastic creation by architect Louis Kahn at eg www.bc.edu/bc_org/avp/cas/fnart/fa267/kahn.html **)**



Salk Institute

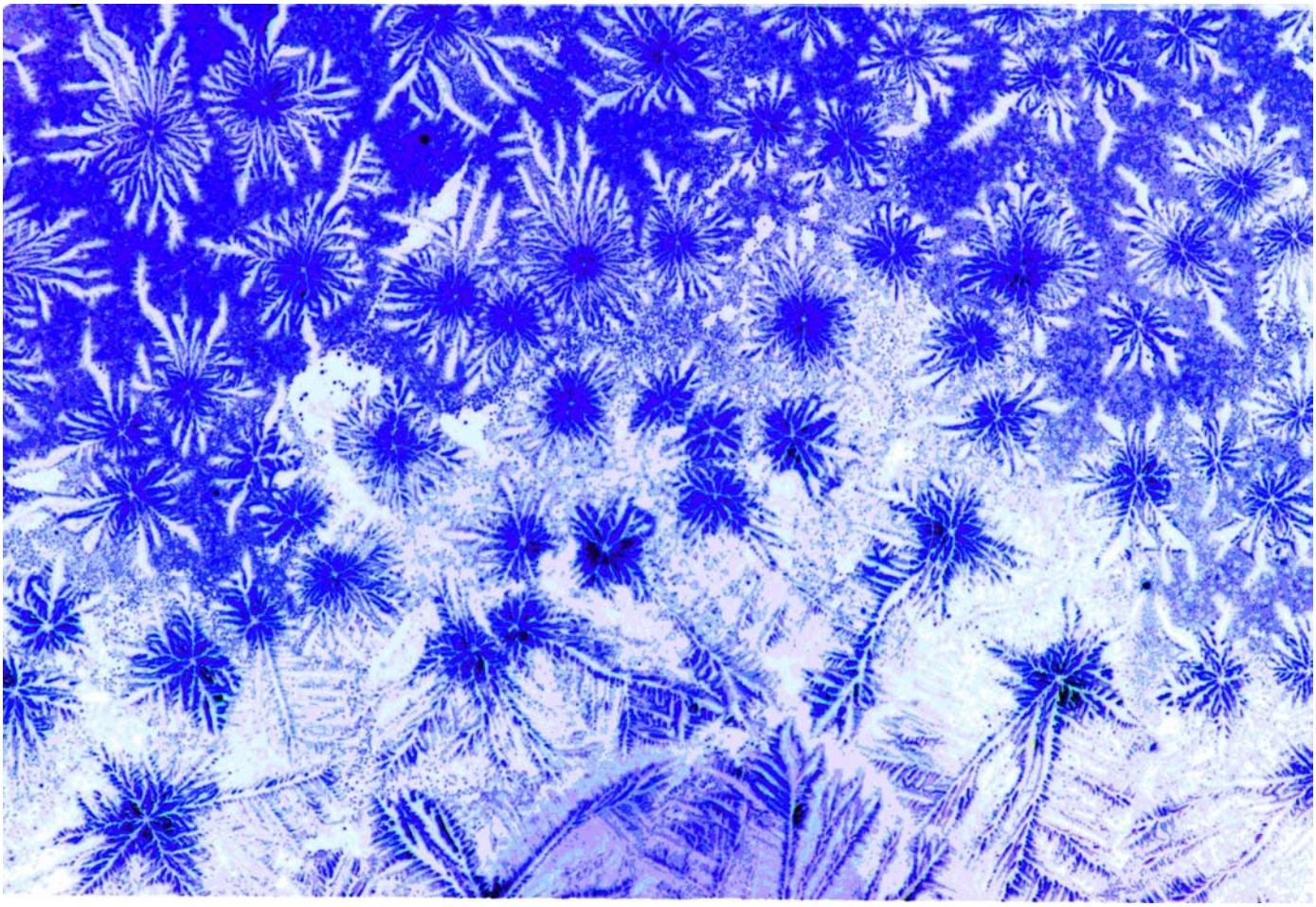
Looking back at the growing crystals: Large needles forming smaller needles, stars forming stars. Fascinating. The patterns of crystals the same but tinier and tinier! Perhaps I should take a picture - and forget the dried up chaotic mess of cells! (I did, see Fig 1). The word "chaos" makes a transient entry into my mind and is gradually substituted by the word "fractals". Isn't that what it is? I need to look "fractals" up on the net!

Google gives me 252.000 hits! Fractals and chaos in business cycles, children's behavior, celestial mechanics, physics, biology, medicine, ecology, economics, chemistry, engineering, and fluid mechanics. Help!! I read "Fractals are geometric objects that look the same on every scale; they arise when we repeat a drawing pattern over and over again, but on even smaller pieces of the picture. A fractal is a shape which is self-similar and has fractional (fractal) dimension, an image that is infinitely complex and self-

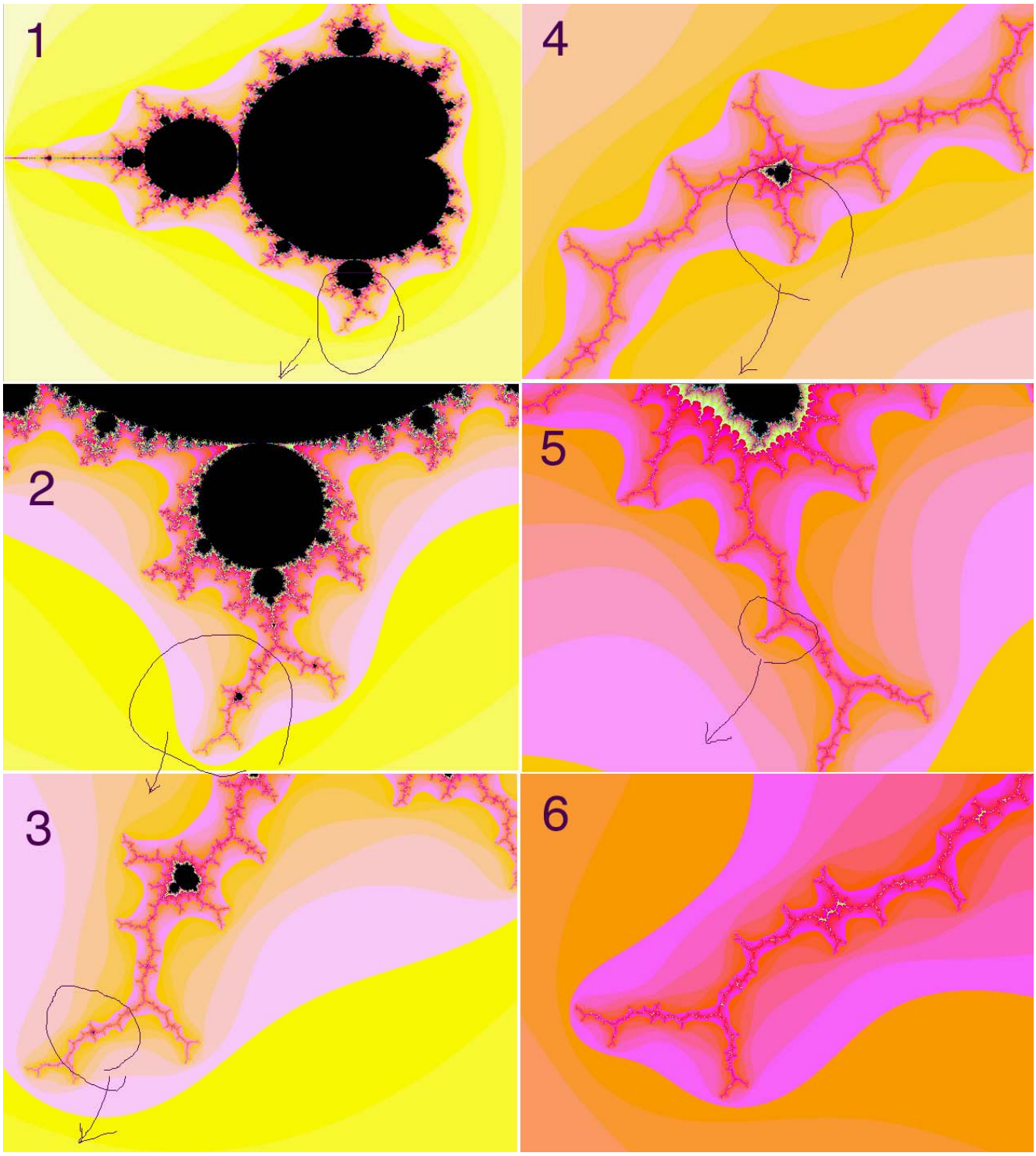
similar at different levels." So I have generated fractals with Dulbecco! I also find a program letting me generate fractals in my computer (www.arosmagic.com;).

Benoit Mandelbrot is the name you stumble on repeatedly. He was born in Warsaw 1924 and moved to France in 1936. Later, he worked at an IBM research center and studied chaotic data in economics. One of the most well known fractal sets, the *Mandelbrot set* "produced by making a map of the behavior of complex numbers as they are fed back from output to input in the equation f(z)=z**2+c." He seems to have a nice example of the consequences of the "fractal nature of nature" How long is the coast of Britain? "The question is less trivial than it seems. Indeed, a dented coast has gulfs and promontories. Each gulf itself is made of smaller bays and each promontory of smaller ones. One can guess that the length found will depend on the degree of detail one has decided to take into account. If, using a map, we survey the coast with 50 km steps (for example using a compass whose pin interval correspond to a 50 km distance) we obtain a certain length. Then we start again with a pin interval corresponding to 10 km, then 1 km (using more and more detailed maps). On can further the reasoning with 100 m steps on an even more detailed map, then we go on the coast itself, supposing that you observe a man walking, then a small dog, and moreover an ant. Every time a bigger length will be found, in inverse ratio to the step used to measure the coast. What is the true length of the coast? The inescapable consequence is that the length of the coast of Britain is infinite."

I happily agree, thinking of those amoebas stretching out their filopodia, even acanthopodia: Measuring the length of coast lines – not only of Britain - would have to take into account these elegant protrusions of their cell membrane! I need to celebrate this insight! Ideally with an almond cookie, but I have to let do with *"Finska Pågar"* (which you can get only in Sweden).



This is what my drying microscope slide looked like!



Ewert Linder

To be able to enjoy the fantastic colors of the photos, please check the pdf file of MTC News at our homepage: http://www.ki.se/mtc/