

# Informati -- on

Ascenion Insight  
November 2012

## 'Clearly clinically relevant'

### Klaus Rajewsky on new animal models for the MGC Foundation

Prof. Klaus Rajewsky has been researching the molecular mechanisms of the immune system for more than 50 years. His work has made a major contribution to the understanding of B-cell function, and has provided new tools for disease research at the molecular level. His research on conditional mouse mutagenesis with colleagues in the 1990s brought him worldwide renown. Over 60 animal models have been developed by his team, and are used by scientists and drug developers all over the world to investigate the molecular mechanisms of various diseases and to test the efficacy of new therapeutic agents.

Together with Ascenion, Klaus Rajewsky founded the MGC (Mouse Genetics Cologne) Foundation in 2006. We talked to Prof. Rajewsky about his motivation, the Foundation and new animal models.

Professor Rajewsky, what was your motivation at the time for setting up the Foundation with Ascenion?

Our mouse models are highly application-oriented. They can help in the development of new medicines that interfere directly in disease processes. The pharmaceutical industry also uses them in preclinical drug development. We wanted to take this opportunity to generate licensing revenues and channel the proceeds back into research. The Foundation allowed us to do this.

Why as late as 2006? The first models date from the 1990s.

When we started on this work, molecular genetics was still in its infancy. It was only after some years that it became practically relevant to the drug development process. Furthermore, we had to solve the distribution problem, also for applications in academic research. We achieved this with the Jackson laboratories, where many of our mouse mutants are kept. Scientists at non-profit-making institutions can obtain the models there free of charge. Industry, on the other hand, must close a licensing agreement with the MGC Foundation through Ascenion.

Around EUR 1 million in licensing revenues have been earned to date.

Where does this money go?

To fund research. The money is distributed according to an allocation key, whereby a proportion goes to the Institute for Genetics at the University of Cologne, where I worked

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for 40 years and developed many models together with colleagues. Another part goes to where my team and I are currently working.

So currently to the MDC in Berlin?

Yes, exactly. And previously to the Immune Disease Institute at Harvard University in Boston, where I moved in 2001, in order to continue working after my retirement.

Are new models from your more recent research included in the MGC Foundation portfolio?

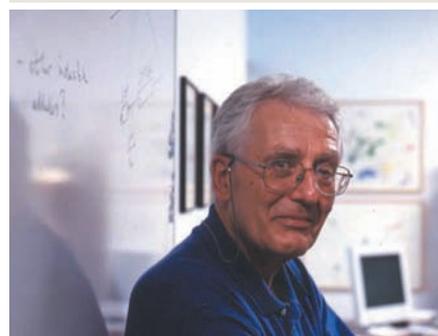
But of course! For example, we have developed a new series of mice that allow the targeted switching on (knock-in) of genes – that is, the opposite of the well-known turning off (knock-out). Some of these mouse mutants have already been published in studies that are clearly relevant to medical problems.

What can be achieved with these new models?

Many of them model signal pathways that are crucial in the development and spread of various types of cancer. They are clearly clinically relevant. Some of them can be used directly for the identification and testing of new therapeutic approaches.

Can you give us an example?

We recently published two new models in *Cell* and *Cancer Cell*. One deals with Burkitt's lymphoma, an aggressive cancer of the lymphatic system that – as we have now shown – is caused by particular molecular changes in B cells. This knowledge of the processes that drive tumour growth opens up new possibilities for drug development. The other model is relevant to tumours that can arise through reactivation of the Epstein-Barr Virus (EBV). Almost every adult over 40 is infected with EBV without knowing it, as the immune system normally keeps the virus reliably under control. In patients with a weakened immune system, however, the virus may reactivate and cause cancer. Using our new mouse model, we have been able to reveal molecular signal pathways that play a crucial role in this process. New therapies could target these pathways directly. This could be an important advance for AIDS patients and transplant recipients.



**Prof. Dr Klaus Rajewsky**

Klaus Rajewsky is currently building the research group 'Immunoregulation and Cancer' at the Max Delbrück Center for Molecular Medicine Berlin-Buch (MDC). The project brings him back to Germany after a 10-year period of research at Harvard University, Boston, USA. He previously worked for nearly 40 years at the Institute for Genetics at the University of Cologne.

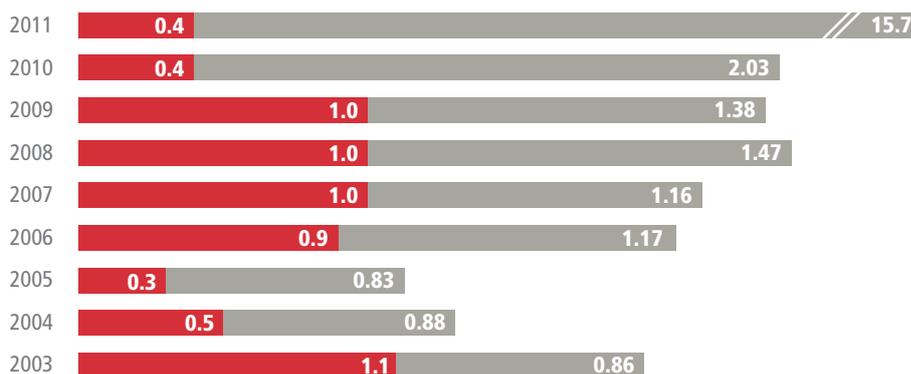
**Details of all the MGC Foundation's animal models are available online at both the Jackson Laboratories and at Ascenion: [www.jax.org](http://www.jax.org) [www.ascenion.de](http://www.ascenion.de)**

## Ascenion in figures

Ascenion achieved record-breaking revenues for its partners in the financial year 2011. 'In technology transfer, individual success stories can quickly boost financial results,' says Dr Christian Stein, CEO of Ascenion. 'What's exciting is that no one can predict which projects will become success stories. The only possible strategy is to bring forward enough good projects each year.' This has allowed Ascenion to achieve continually rising returns for its partners over the years.

Partners' revenues include income from agreements negotiated by Ascenion, as well as surpluses from its equity and operative activities that Ascenion has paid out to the LifeScience Foundation. These proceeds are made available to the founding institutions to fund further research.

Revenues for Ascenion's partners (million EUR)



■ Proceeds forwarded by Ascenion to the LifeScience Foundation ■ Revenues from agreements

## Ask the inventor



### **Prof. Dr Klaus Brandenburg**

(back row left) and his spin-off team, Priority Area Infections / Biophysics  
Research Center Borstel – Leibniz Center for Medicine and Biosciences

For many years, Klaus Brandenburg and his team have been researching sepsis – a medical condition of which there is very little public awareness, despite the alarming statistics: in Germany alone, it is responsible for 160 deaths a day. Sepsis is caused by ‘bacteria in the wrong place’. Just a millionth of the bacteria present in the intestines is enough to cause a septic shock if it gets into the bloodstream. Septic shock is triggered by endotoxins, a group of biomolecules bound to the bacterial cell membrane. They stimulate the immune system so powerfully that it can run out of control. Killing the bacteria – for example with antibiotics – is not sufficient to curb the immune response. It is often even counterproductive, as the destruction of bacteria increases the concentration of endotoxins in the blood. Klaus Brandenburg and his team have therefore developed a novel peptide for the treatment of sepsis that binds bacteria and simultaneously neutralizes their endotoxins.

**My first experience of technology transfer was...**

...when I presented our results to staff at Ascenion in the summer of 2007, in order to discuss whether it was worth applying for a patent. Our peptide was considered to be patent-worthy, and that was the beginning of our collaboration. Parallel to preparing the patent application, we looked for partners and financing opportunities in order to advance the project. Just one day after submitting

the patent application, we submitted an application for funding to the German Federal Ministry of Education and Research (BMBF), together with the RWTH Aachen and Hannover Medical School (MHH), which was subsequently granted. Since then, the project has made huge strides. We have just had some very positive preclinical results in animal models of peritonitis.

**What surprised me most...**

... was the passive attitude of the pharmaceutical industry. Our project addresses a tremendous clinical need that appears to be growing. There isn't a single effective therapeutic agent for sepsis, and hundreds die from it every day. We have spoken to suitable companies but haven't met with any readiness to invest money and take up the project – despite its huge innovation potential. Not yet, at least. They want to see ‘clinical proof-of-concept’ first – that is, evidence that the treatment works in humans. On the one hand this is understandable, as many pharma industry development projects in sepsis have failed dramatically. On the other hand, our approach is based on a completely different and much more fundamental concept that is more likely to be effective. But the reluctance remains.

**I think the biggest hurdle for technology transfer is...**

... a double one! Firstly money: the pharmaceutical industry only gets on board when

the project is at an advanced stage of development, preferably already at the clinical stage. But who pays for development up to this point? The funding via the BMBF Program that benefitted us at the beginning has now finished. We are currently applying for funding from the EU's FP7 Program and plan a spin-off. But for this we also need investors. The second hurdle is the enormous challenge facing the scientists involved. Project development starts where every ‘normal’ scientist bows out: you have to get to grips with countless international regulations, standardized processes, etc. It all takes a lot of energy!

**My personal gain from technology transfer is...**

... not easy to formulate. You arrive at a completely different level and see your work from a new perspective. My personal gain will be greatest when we succeed together in developing a therapy.

**If I could choose one project that would reach the market, it would be...**

... our peptide for the treatment of sepsis. This would be a huge advantage for many patients. Then there are the ‘accidental’ products of our research on the peptide. We have discovered that it has antiviral effects – for example, against the influenza virus variant H1N1 that is capable of causing a worldwide epidemic. It can also bind to multi-resistant bacteria that have become a serious threat to public health.

## News from the Spinovator

### **Further partners und projects**

Ascenion, Vesalius Biocapital and the German Federal Ministry of Education and Research (BMBF), are opening the Spinovator to further venture capital companies and research institutes. The new financial instrument is now available to investors with

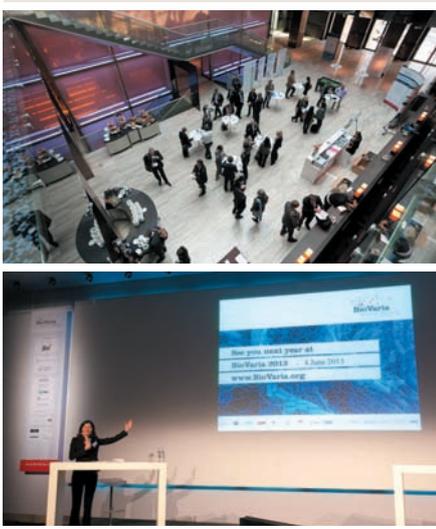
a fund in the investment phase who wish to actively participate in the development of early-stage projects. In addition, institutes other than Ascenion's partner institutes may now apply for funding for their projects. With this move, the Spinovator's three founders

are responding to the high level of interest shown by other parties. New potential investors to date are Biogeneration Ventures, Creathor Venture, Forbion Capital Partners, LSP, Peppermint VenturePartners and TVM Capital Life Science.



## Networks

### For licensees and licence suppliers: BioVaria 2013



The 6th BioVaria will take place on 4 June 2013 in Munich. BioVaria is the only European technology transfer event that brings scientists and transfer organizations from all over Europe together with scouts and investors from the pharmaceutical industry. This year, 13 technology transfer organizations presented over 50 commercially attractive life-science projects from 46 research institutes and universities in nine countries. The event met with a lively response from the biopharmaceutical industry. 'One of BioVaria's biggest advantages is the quality of its participants: here you can find first-class industry representatives and venture capitalists, as well as Europe's leading technology transfer

organizations,' commented Dr Stéphane Mottola from the French technology transfer organization FIST. The tried-and-tested format of short presentations, a poster exhibition and opportunity for individual discussions will be continued in 2013. As previously in 2011, there will again be a Spin-off Panel at which European entrepreneurs can present their projects to a jury of top venture capitalists in an interactive format.

Ascenion hosts BioVaria in cooperation with its technology transfer partners. More information on participating as a partner, spin-off or sponsor under [www.biovaria.org](http://www.biovaria.org) or contact Esther Lange, T +49 89 318814-22, [lange@ascenion.de](mailto:lange@ascenion.de)

## Spinning Innovation

### Systems biology for market makers

Clueda AG, the latest spin-off from the Helmholtz Zentrum München, develops innovative software for associative knowledge processing and analysis. Unique algorithms – inspired by systems biology – screen, structure and analyse vast amounts of data from varied sources to reveal relevant relationships that would normally be inaccessible in the data flood.

Clueda has already established proof-of-concept in the healthcare field. Using its software, physicians can draw valuable information from patient data collected over years, for instance on co-morbidity or on the efficacy and possible side-effects of treatments. Now, the company plans to extend its approach to the financial sector. Ascenion spoke to Christian Bacherl, Co-Head of Corporates and Markets at Baader Bank, Clueda's seed investor and strategic partner:

This is the first time that Baader Bank has made an early-stage life-science investment. Have you entered the venture capital business? Certainly not. Baader Bank is – and will continue to be – a leading investment bank and market maker in Germany. Our partnership with Clueda is of strategic nature. We have a vital interest in developing their technology for financial market applications.

#### Why?

As market maker we quote some 500,000 financial instruments per day. Our team has to screen, consolidate and analyze endless bits and pieces of information each day. Given the growing flood of data, we have long been looking for a tool to support us in information management. Our goal is twofold: firstly, we want to reduce the time we spend gathering information, and secondly, we want to make sure that we instantly identify significant events or 'soft information' that will impact the markets.

What convinced you of Clueda's approach? We have been in contact with many players in the field, including the market leaders. During our search, we also came across Clueda's tool, which seemed to us to be the most promising. Clueda's semantic software not only gathers information, but also structures and evaluates it in a similar way to the human brain. This could be extremely helpful.

#### Why did you choose a dual role as client and investor?

We believe this is the most effective way to help the company get off the ground and make its technology available for multiple applications.

Clueda is at an early stage, and so is the software with regards to financial market applications. We are looking forward to working closely with the team and developing its organization and products step-by-step towards the market.

### Editorial

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