Researchers successfully develop animal free methods for testing chemical compounds for allergens, ahead of the EU ban

EU-funded research project developing *in vitro* ('out of body') test strategies to reduce or replace animal testing use gene expression analysis software

As of march 2013 there is a ban in the European Union (EU) on animal testing of ingredients for cosmetics. The ban applies to all new cosmetics and their ingredients sold in the EU, regardless of where in the world testing on animals was carried out. The 27 EU countries have had a ban on such tests in place since 2009, but despite this, cosmetics firms were allowed to continue testing on animals for the most complex human health effects, such as toxicity which might lead to cancer. However, those tests now come under the ban too.

This controversy has resulted in research to produce new, animal free, testing methods for chemicals. One such research initiative involved was Sens-it-iv (www.sens-it-iv.eu), a large EU-funded research project dedicated to develop and optimise *in vitro* ('out of body') test strategies that could reduce or replace animal testing for sensitization studies. In 2005, lead by Malin Lindstedt, at the Department of Immunotechnology at Lund University, Sweden, and professor Carl Borrebaeck, Vice Chancellor of Lund University and sub-coordinator of Sens-it-iv, Lindstedt's group joined with Sens-it-iv. At this time there were no animal free methods for testing chemical compounds for their potential to induce allergies on the market.

One of the key partners involved with the project was the European Centre for the Validation of Alternative Methods (ECVAM) at the Joint Research Centre in Ispra, Italy. As a result of this co-operation, Lindstedts' group in Lund has now developed a completely animal free method based on human cells grown in the lab.

Dr. Ann-Sofie Albrekt, the bioinformatician in the team, has done a substantial amount of the analyses for the Sens-it-iv project and the further development of the animal free assay, named GARD (Genomic Allergen Rapid Detection). As an internationally-renowned centre for research and education, Lund University is highly regarded for its research in cutting-edge fields including nanotechnology, translational cancer research, and stem cell biology. Dr. Albrekt is currently focusing on two key areas: looking for new biomarkers in cancer studies, as well as performing important research on allergens.

"Worldwide, more and more people are suffering from allergies, which means that this area has become an important health concern," says Dr. Albrekt. "As a scientist, I am interested to

find out why otherwise harmless compounds can often elicit an adverse immune response in humans."

Making sense of important data

Dr. Albrekt is currently using sophisticated data analysis software, called Qlucore Omics Explorer, to help her to get the most value out of the data being produced by this research.

"Although gene expression studies are proving invaluable to the study of allergens, the amount of data that is produced by these experiments is enormous," she says. "As a result, it is impossible to derive any real biological meaning from these findings unless sophisticated data algorithms are used to help interpret this data effectively."

For this reason, most of the software that has been designed for use in this area has mainly focused on the ability to handle increasingly vast amounts of data, which means that the role of the scientist/researcher has been largely set aside. As a result, a lot of data analysis has been passed on to bioinformaticians and biostatisticians. However, in most cases, this model has several drawbacks, since it is typically the scientists themselves who know the most about biology.

"In our studies, we are dealing with very large amounts of data, sometimes between 10 and 100 million data points, which we tend to view as graphics" says Dr. Albrekt. "With other software, these graphics would take a long time to appear, but with the latest data analysis tools, the information is presented instantly. As a result, we can be much more creative with our theories, as we can easily test any number of hypotheses in rapid succession."

With the freedom, speed and flexibility provided by this approach, it is now possible to evaluate and test a number of different scenarios and hypothesis in a very short time, and to fully understand the data being examined. This technique makes it possible for researchers to combine very large amounts of data, and therefore to conduct analysis in ways that were simply not possible before.

The future

The latest technological advances in this area are making it much easier for researchers to compare the vast quantity of genomic data generated, to test different hypotheses, and to explore alternative scenarios within seconds. Not only that, but the latest generation of data analysis software is also helping the scientists (biologists, MD, and so on) to regain control of the analysis and to realise the true potential of gene expression profiling.

According to Dr. Albrekt, her own research efforts will continue to focus on both the allergen studies, as well as on the ongoing cancer research within CREATE Health, which is a strategic centre for translational cancer research.

"In terms of the work we did in the Sens-it-iv project, I am very confident that our success in creating an animal free test system will significantly reduce the number of animals sacrificed for safety testing and as well as increasing the accuracy of the safety tests performed " she says. "This project will therefore be of substantial benefit to all European citizens, and that goal continues to motivate me to make new discoveries in this area."

The assay development work resulting in the GARD assay will be presented in the doctoral thesis defense of Henrik Johansson on June 5th at Lund University.

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About Qlucore
Qlucore started as a collaborative research project at Lund University, Sweden, supported by researchers at the Departments of Mathematics and Clinical Genetics, in order to address the vast amount of high-dimensional data generated with microarray gene expression analysis. As a result, it was recognised that an interactive scientific software tool was needed to conceptualise the ideas evolving from the research collaboration.

The basic concept behind the software is to provide a tool that can take full advantage of the most powerful pattern recogniser that exists - the human brain. The result is a core software engine that visualises the data in 3D and will aid the user in identifying hidden structures and patterns. Over the last few years, major efforts have been made to optimise the early ideas and to develop a core software engine that is extremely fast, allowing the user to interactively and in real time instantly explore and analyse high-dimensional data sets with the use of a normal PC.

Qlucore was founded in early 2007 and the first product released was the "Qlucore Gene Expression Explorer 1.0". The latest version of this software, now called "Qlucore Omics Explorer 2.0", was released in May 2009, and represents a major step forward with the added support for hierarchical clustering, scatter plots and powerful log function. The combination of instant visualisation and advanced statistics support gives the user new opportunities. All user action is at most two mouse clicks away. The Company's early customers are mainly from the Life-science and Biotech industries, but solutions for other industries are currently under development.

One of the early key methods used by Qlucore Gene Expression Explorer to visualise data is dynamic principal component analysis (PCA), an innovative way of combining PCA analysis with immediate user interaction. Dynamic PCA is PCA analysis combined with instant user response, a combination which provides an optimal way for users to visualise and analyse a large dataset by presenting a comprehensive view of the data set at the same time, since the user is given full freedom to explore all possible versions of the presented view. Later versions combine PCA analysis with other analysis methods such as hierarchical clustering.

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