Australian Galactosaemia Support Network

Galactosemia Foundation Conference 2012

Research Update

In the world of medical research there are often several teams chasing many leads and possibilities when trying to cure or development treatments for a particular condition at any one time. This is certainly the case with galactosaemia. The conference featured a number of presentations from different research teams that have differing views of how treatments for galactosaemia will be developed. Some of these views complement each other. However, some views contradict each other and it is important to understand that although this is the case all of the researchers involved are working towards the same goal and are following the leads which they consider to be the most likely to succeed. We are lucky to have these impressive and dedicated research teams working to help us and the AGSN is committed to helping them where possible.

The science behind the research is very complicated and can be confusing. In the summaries below we have not gone into full detail of all of the studies and testing that has been undertaken, but have attempted to convey the key messages as they were conveyed at the conference. If anyone would like more detail on the research please email us at agsn@agsn.org.au and we will help to the extent possible by pointing you in the direction of the relevant research papers and other materials.

We have also not detailed the science behind galactosaemia in this update. If you want more detail on this the best place to start is on page 12 of the ASIEM Handbook for Galactosaemia.

Possible cures for galactosaemia

The presenters at the conference discussed the likelihood of cures for galactosaemia being developed. At the moment complete cures are still some way off. Although research teams are gaining a better understanding, galactosaemia is an incredibly complex condition and the answers to the questions it poses are not easily solved. Some teams are working on galactokinase inhibitors that could be developed into drugs which have the effect of reducing or stopping production of galactose-1-phosphate, while others are turning their attention to gene therapy. Both are discussed further below.

Galactokinase inhibitors

The enzyme galactokinase is used by the body to convert galactose into galactose-1-phosphate. This is the first step in the overall conversion of galactose into glucose. The thinking behind the research in this area is that if galactokinase is prevented from operating to convert galactose into galactose-1-phosphate, the subsequent build up of galactose-1-phosphate seen in galactosaemia patients will not occur. These researchers believe that by reducing the presence of galactose-1-phosphate in patients many, if not all, of the symptoms of galactosaemia will be avoided. The inhibition of galactokinase is not considered to be a risk as people living with the condition galactokinase deficiency do not experience problems to the extent seen in galactosaemia.

The research in this area, led by Dr Kent Lai of the University of Utah, has developed to the point where animal trials are required. Dr Lai has developed a mouse model on which potential drugs could be tested. However, in order to proceed with these trials Dr Lai's team needs further funding, which will hopefully come from the pharmaceutical companies that would produce any drug that is ultimately developed. The exciting part about this research is that Dr Lai has also shown that galactokinase inhibitors could be used to kill cancer cells, thereby increasing the chances that pharmaceutical companies will be prepared to invest in his research. Dr Lai estimates that if he were to receive sufficient funding and further trials are successful, a drug could be available in the market in about five years.

We should note that some presenters at the conference, particulary Dr Judith Fridovic-Keil of Emory University, expressed doubt about the effectiveness of galactokinase inhibitors on the basis of research that has been undertaken independent of that undertaken by Dr Lai's team. Dr Lai is aware of those views and still considers his path to be valid. We express no view on which path is correct or which is more likely to succeed.

Gene therapy

Gene therapy is a relatively new form of science in which a person's genetic structure can be altered to address mutations that cause that person to suffer from a certain condition. Genetic conditions such as galactosaemia are thought to be ideal for treatment via gene therapy.

However, the process for developing a cure for galactosaemia through gene therapy will be long and, given the length of the process, success is not certain. This work will also be expensive and scientifically complex.

As galactosaemia is a rare and complicated condition, a significant amount of background work needs to be undertaken before scientists and doctors are able to launch into development of treatments. Doctors are currently working on putting together a global database of patients with galactosaemia which will be available to assist with research in this area. This was described as the top research priority for the team led by Dr Gerard Berry of Harvard Medical School

and it is intended that this database will include patients from Australia. The development of the database is supported by the US National Institute of Health.

The information on the database will include details such as the specific mutations seen in each patient and the symptoms experienced by each patient. This will hopefully give the researchers the ability to identify why some people with galactosaemia suffer severe symptoms and why others show almost no symptoms. Once that identification has been made, gene therapy may be able to be used to aid those who are more severely affected.

Another challenge in developing gene therapy is that galactosaemia specific stem cells need to be created which can then be used to test and develop potential therapies. Dr Berry's team have been able to successfully develop these cells and are now ready to start working to test and develop therapies in conjunction with the research that will be performed once the international database is established.

Other ongoing research

Dr Judith Fridovich-Keil's team are working with both yeast and fruit fly models to further our understanding of galactosaemia. Their work focusses on identifying when and where in development damage caused by galactosaemia occurs. Some of the doctors present at the conference suggested that the damage may occur either before or shortly after birth, even though it may take many years for the symptoms (such as speech difficulties or tremors) to manifest. Dr Fridovich-Keil has also been doing work in relation to ovarian function, which will be discussed in more detail in our update on reproductive issues.

Dr Susan Waisbren of Harvard Medical School and her team are performing research into the neurological aspects of galactosaemia. In particular, they are using advanced MRI scanning to analyse neural pathways in adults with galactosaemia. To date this research has shown that galactosaemia appears to damage the right side of the brain and, therefore, the symptoms of galactosaemia are largely to do with reduced right side brain function. The good news is that early intervention can help to address this.

As a point of interest, the AGSN is currently working with a team of researchers in Australia who are also investigating neural pathways in galactosaemia and trying to develop early testing for abnormal neural pathways in children. This shows that the research being conducted in Australia is cutting edge and that Australia can make a significant contribution to research, provided we can raise sufficient funds to keep the research going in coming years (as government support is often limited).