IARC 2015 Lay Summary Session 3a: Cellular & Animal Models in Friedreich's ataxia

Much of our knowledge about human genetic diseases has been obtained by studying cellular and animal models. They can reproduce clinical symptoms and mimic states of the diseases. Therefore, these models are very valuable for understanding the development of the disease and investigating new pharmacological or genetic treatments.

Session 3 was an interesting session of talks regarding the state and recent advances of the disease models that are currently used in the study of Friedreich ataxia (FA), a neurodegenerative disease caused by a reduction in the correct functioning of the protein frataxin. Dr. Helene Puccio (IGBMC, France) started with a presentation summarizing the contribution of the mouse models generated in her laboratory to understanding the physical symptoms of FA. She also talked about a new mouse model that displays a reduction of frataxin production in specific tissues. This causes many of the symptoms of the disease, improving previous models that only expressed some symptoms of FA. Progress in this model will allow more in-depth studies on the progression of the disease in animals.

An interesting FA mouse model was introduced by Dr. Vilayendran Chandran (UCLA, USA). In this model, it is possible to reduce the production of frataxin in the whole organism by the administration of the compound doxycycline.

What makes this model remarkable is that it is possible to restore the normal production of frataxin after the levels of the protein have been reduced, simply by stopping the doxycycline treatment. This system allows researchers to study the reversibility of symptoms at different stages of the disease and to investigate the critical developmental period when frataxin is essential.

Regarding cellular models, Dr Simona Donatello (Université Libre de Bruxelles, Belgium) showed the work that her group has been doing with induced pluripotent stem cell-derived neurons obtained from patients, a model that is useful both to study the alterations caused by frataxin reduction and to test therapeutic compounds.

Other models shown at the conference are valuable tools to identify promising therapies based on the recovery of frataxin levels (allowing for frataxin to be made normally), and acting on gene silencing mechanisms mediated by the GAA expansions in the *FXN* gene. GAA expansion is a type of mutation whereby the trinucleotide GAA is repeated many times in the genome, causing a reduction in the frataxin produced.

Dr Michele Lufino (University of Oxford, UK) described cellular and mouse models with a GAA expansion mutation to study how frataxin production is decreased in FA, and to screen molecules able to increase the expression of this protein. Showing the utility of these models, he showed examples of such molecules that his group had discovered. Dr. Josep Llorens (Universidad de Valencia, Spain) also presented an interesting model developed in *Drosophila* to study the effect of the GAA expansion.

Overall, session 3a proved to be very successful in displaying new models for studying Friedreich's ataxia, which will hopefully lead to substantial progress in research, particularly in finding specific treatments.

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