Protein findings open new avenues to understanding and treatment of schizophrenia

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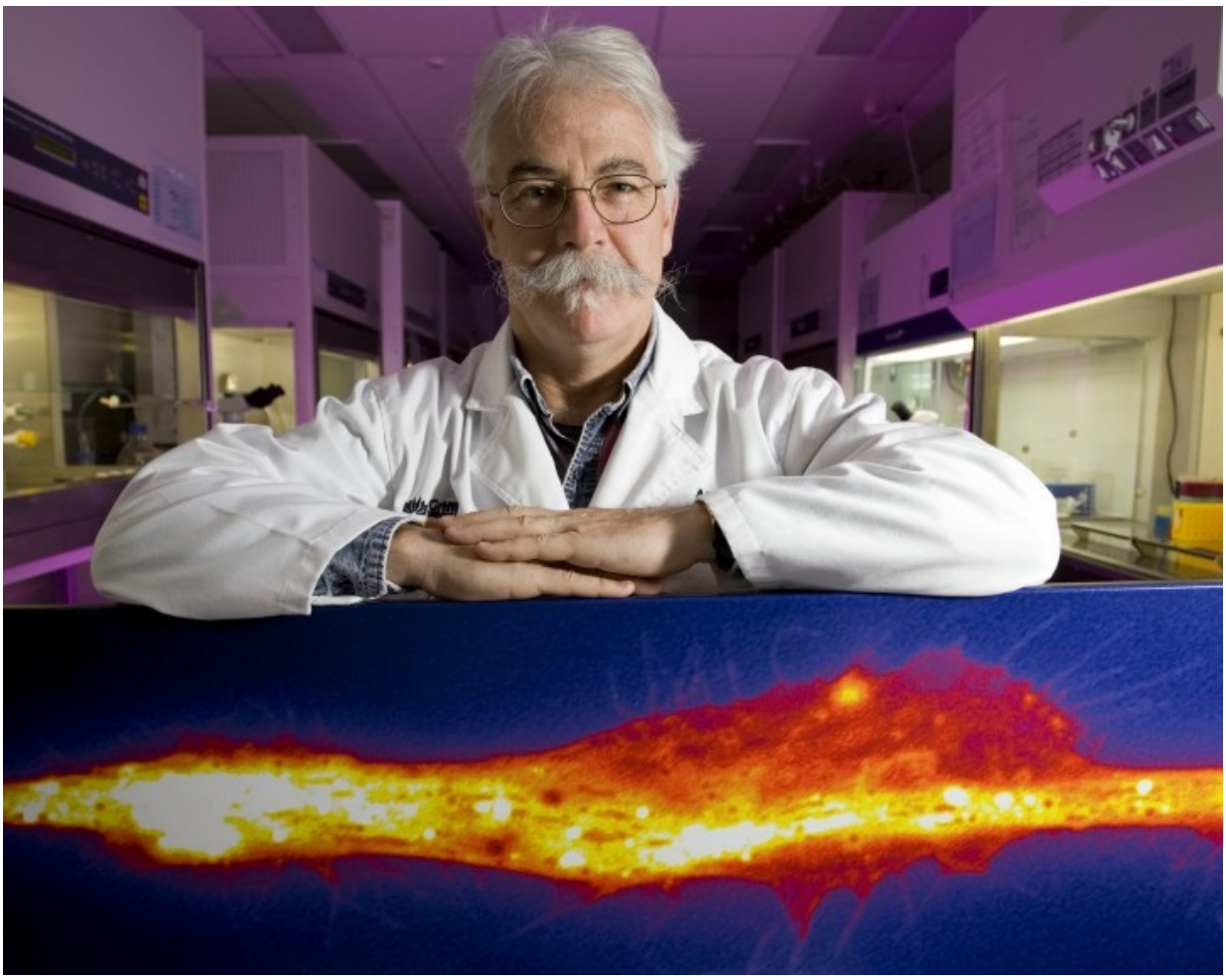

Professor Alan Mackay-Sim, from Griffith University's Eskitis Institute for Drug Discovery is pictured. Credit: Griffith University

Stem cells from adult schizophrenia patients form new proteins more slowly than those from healthy people, according to new research.

The findings are enhancing understanding of how schizophrenia affects the workings of the brain, and open the way to new approaches for future drug therapies.

Involving scientists from Griffith University's Eskitis Institute for Drug Discovery, the Royal College of Surgeons in Ireland and University College Dublin, the research is published online in the journal *Translational Psychiatry*.

According to the Eskitis Institute's Professor Emeritus Alan Mackay-Sim, analysis of almost 1000 proteins in patients' stem cells indicated their cellular machinery for making new proteins was reduced, with the rate of protein synthesis greatly impaired.

"Proteins are the workhorses of all cells and make up most of a cell's structure and functions," says Professor Mackay-Sim, whose Griffith team included Dr Yongjun Fan and Mr Nicholas Matigian.

"Cells live in a very dynamic environment and protein synthesis, which is so important for brain development, function and learning, is impacted by environmental and genetic factors.

"It is now becoming clearer that many small genetic variants are linked because they share control of cellular functions, in this case protein synthesis.

"If protein synthesis is altered even slightly, many cell functions would also be subtly changed. This could affect brain development and adult brain function in schizophrenia.

"This work helps make sense of the rapid advances in genetics that have identified hundreds of risk genes for schizophrenia."

Interestingly, the same issue of *Translational Psychiatry* reports contrasting findings from a second research collaboration, also involving Professor Mackay-Sim, University College Dublin and a laboratory in the US.

This study used a different kind of stem cell generated from people with schizophrenia, namely induced pluripotent stem cells.

These are genetically engineered from skin cells and stimulated to turn into stem cells resembling the neural progenitor cells that give rise to the brain in the developing human embryo.

When the proteins from these cells were analysed, the patients' cells were found to have more protein-making machinery and also made proteins more quickly than cells from healthy controls.

"However, while on the surface this seems like a contradiction, the two studies support each other by showing that the regulation of protein synthesis is subtly disturbed in the cells of people with schizophrenia," says Professor Mackay-Sim.

"The studies seem to show that the on/off switch for protein synthesis may be altered in different cells or at different life stages in schizophrenia.

"This provides many ways in which brain development and function is altered in schizophrenia, and many routes for the ways in which genes and the environment interact to cause schizophrenia."

More information: J A English et al. Reduced protein synthesis in

schizophrenia patient-derived olfactory cells, *Translational Psychiatry* (2015). DOI: 10.1038/tp.2015.119