Cell binding discovery brings hope to those with skin and heart problems

January 21 2011

A University of Manchester scientist has revealed the mechanism that binds skin cells tightly together, which he believes will lead to new treatments for painful and debilitating skin diseases and also lethal heart defects.

Professor David Garrod, in the Faculty of Life Sciences, has found that the glue molecules bind only to similar glue molecules on other cells, making a very tough, resilient structure. Further investigation on why the molecules bind so specifically could lead to the development of clinical applications.

Professor Garrod, whose Medical Research Council-funded work is paper of the week in the Journal of Biological Chemistry (*JBC*) today, said: "Our skin is made up of three different layers, the outermost of which is the epidermis. This layer is only about 1/10th of a millimetre thick yet it is tough enough to protect us from the outside environment and withstand the wear and tear of everyday life.

"One reason our epidermis can do this is because its cells are very strongly bound together by tiny structures called desmosomes, sometimes likened to rivets. We know that people who have defects in their desmosomes have problems with their epidermis and get extremely unpleasant skin diseases. Understanding how desmosomes function is essential for developing better treatments for these and other types of skin disease and for non-healing wounds.

"Desmosomes are also extremely important in locking together the muscle cells of the heart, and hearts where desmosomes are defective can fail catastrophically, causing sudden death in young people.

Hence our findings may also be relevant in the heart and in developing new treatments for heart disease."

ProfessorGarrod and his team, Zhuxiang Nie, Anita Merritt, Mansour Rouhi and Lydia Tabernero, used chemical cross-linking to study cells of the epidermis and found what they believe to be the principal mechanism by which the glue molecules of desmosomes of skin cells bind to each other.

"For reasons that we do not fully understand there are several different but closely-related glue molecules within each desmosome," he explained.

"Our results show that each glue molecule on one cell binds primarily to another of the same type on the neighbouring cell, meaning the binding is highly specific. This was very surprising because previous studies using different techniques had not been able to give such a clear answer on the specificity of binding."

He added: "Our result suggests that this type of specific binding is of fundamental importance in locking together cells of the epidermis into a tough, resilient structure. It is an important step forward in our research, which aims to develop better treatments for non-healing wounds, other skin diseases and heart problems. We could do this if we understood how to make medicines that would lock or unlock the desmosomes as required."

More information: 'Membrane-impermeable crosslinking provides evidence for homophilic, isoform-specific binding of desmosomal

cadherins in epithelial cells' is published in the *Journal of Biological Chemistry.*

Provided by University of Manchester