Revolutionary discovery could help tackle skin and heart conditions

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Scientists at The University of Manchester have made an important discovery about how certain cells stick to each other to form tissue.

The team from the Faculty of Life Sciences studied how cells in the skin and heart are bound together through structures called desmosomes. They wanted to understand how these junctions between the cells in the tissue are so strong.

Desmosomes are specialised for strong adhesion. They bind the tissue cells together to resist the rigours of everyday life and their failure can result in diseases of the skin and heart, including sudden cardiac death.

Contrary to popular scientific thinking the researchers revealed a revolutionary finding – that the desmosomes achieve their strength through flexibility rather than rigidity. Their findings have been published in the journal *PNAS*.

Dr Lydia Tabernero explains the results: "Scientists had always thought the reason for these incredibly strong connections was because the molecules were very rigid and structured as they are in other, weaker intercellular junctions. However, when we isolated desmosome molecules and characterised them we found that they are actually much more flexible than those of the other junctions – the total opposite to what people had thought!"

Desmosomes contain proteins that have extra cellular regions. These form the adhesion that bind the cells to each other and prevent them from separating.

To study their structure Dr Tabernero and her team extracted the proteins and accessed the molecules. Using x-ray scattering, biophysical and computational analyses they were able to build a model of what the molecule looks like and reveal its flexible nature. The molecules are much more ordered than in other intercellular junctions and the ordering is crucial for strong adhesion. Curiously, it is this flexibility that enables them to become ordered.

Dr Tabernero comments: "What is really fascinating about desmosomes is that they become weaker during wound healing and embryonic development, and this weakening is necessary to allow cells to move. In contrast, desmosomes are very strong in adult tissues, particularly in skin and heart. It has been incredibly difficult to work out how they do that but our findings shed new light on this."

She continues: "Conducting this research has been very challenging, but understanding the result was even harder as it went against everything we were expecting. Seeing the flexibility was a big surprise and we had to retest the molecules using different techniques to confirm our findings."

Professor David Garrod has studied desmosomes for decades. He says there are exciting implications for these findings: "This is the first time that any structural information has been reported for desmosome adhesion. Understanding these cell junctions will be important for future biotechnology applications. We also hope our research will contribute to studies into wound healing, cancer and embryonic development."

More information: "Cadherin flexibility provides a key difference between desmosomes and adherens junctions." *PNAS*. DOI: 10.1073/pnas.1420508112

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