Scientists eavesdrop on the exciting conversations within cells

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Scientists have discovered the secrets of a sophisticated molecule that plays a role in many aspects of human health from fertility to blood pressure; digestion to mental health. This has opened up the potential for discovery of new drugs to treat an enormous variety of conditions.

In research supported by the Biotechnology and Biological Sciences Research Council (BBSRC) and the Wellcome Trust a team from the University of Cambridge shows how a molecule - the IP3 receptor - arranges itself into clusters to help broadcast vital chemical messages around cells in the form of calcium. The work is published today (25 February) in *Nature*.

Team leader, Professor Colin Taylor said: "Almost everything a cell does is regulated by calcium, and we know there are many diseases in both humans and animals, such as stroke or an irregular heart beat, in which calcium regulation goes wrong. But the real puzzle is trying to understand how calcium - which is amongst the simplest of all chemicals - can manage to control lots of different things at the same time. What we have found is a crucial part of that puzzle.

"Imagine you're trying to find a dancing partner at a party. You might whisper the request to several people, or you might shout it out to everyone. Some of your handful of whispered requests might be ignored and some may have you heading for the dance floor. If you shout loud enough, everyone gets to decide whether to respond. It's rather similar with messages transmitted by calcium signals: they can evoke very

different responses in cells depending on whether they are whispered or shouted."

The research published today shows that when cells are stimulated, their IP3 receptors receive instructions telling them to both gather into clusters and to open and allow calcium to pass. Furthermore, IP3 receptors behave very differently when they are alone as opposed to clustered, and these differences help determine whether the calcium signal is "whispered" or "shouted".

Professor Taylor continued: "The IP3 receptors that we work on are interesting because we've found that they can both whisper and shout. Lone IP3 receptors whisper, but when they get together they can shout - not just because their combined effort is bigger, but because the calcium they release stimulates their neighbours to release calcium as well.

"We need to understand fully how IP3 receptors work if we are to begin to think of them as future targets for drugs. The clustering that we have observed fills an important gap in this understanding and takes us a step closer to being able to design drugs for a number of important diseases where we know calcium regulation goes wrong."

Professor Janet Allen, Director of Research, BBSRC said: "There is still an awful lot we don't know about the way healthy humans work. Until we get to the bottom of how complex biological processes work, what it is about them that maintains health, and where the potential points of intervention might be when things go wrong, there will be many diseases that we will not be able to treat effectively. It is reassuring to see fundamental work going on that can deliver answers to these questions. We are delighted that Professor Taylor's group have been recognised for their achievements in this area and congratulate them on publication of their *Nature* paper."

More information: *Nature*, doi:10.1038/nature07763

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