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Researchers find signal that switches on eye development -- could lead to 'eye in a dish'

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Researchers at the University of Warwick have uncovered a crucial signal that switches on eye development. This discovery will greatly assist researchers looking at stem cells connected to eye development and opens up an avenue of research that could eventually lead to an “eye in a dish”.

The University of Warwick research team led by Professor Nick Dale and Professor Elizabeth Jones from the University of Warwick’s Biological Sciences Department have published their work today, 25th October 2007, in *Nature* in a paper entitled Purine-mediated signaling triggers eye development.

The researchers were exploring whether release of ATP (an important signaling and energy carrying molecule) influenced the development of locomotion in frogs. Their experiment introduced molecules called ectoenzymes (normally found on the outside surface of cells) into frog embryos at one of the earliest stages when the frogs-to-be were just 8 cells in size. Three ectoenzymes were used: E-NTPDase1, E-NTPDase2 and E-NTPDase3. These ectoenzymes degrade ATP following its release from cells, however each version of the ectoenzyme has slightly different effects on this degradation.

The Warwick research team’s interest in locomotion was quickly eclipsed when they were amazed to find that the introduction of just one of the ectoenzemes (E-NTPDase2) had a dramatic affect on eye development in the tadpoles grown from these embryos. When

introduced in cells that would form the head area of the tadpole multiple eyes appeared to be created. That was not the only surprise. When it was introduced in some cells that formed body parts outside the head area it could still produce an additional “ectopic” eye leading to tadpoles with an additional eye in their side, abdomen or even along their tail.

E-NTPDase2 quickly latches on to ATP converting it to ADP. This meant that where and when the researchers introduced E-NTPDase2 it led to nearby cells experiencing much higher levels of ADP. The Warwick team hypothesized that ATP must be released in a short burst from the location where the eye will develop so that it can be converted to ADP by E-NTPDase2, thereby providing the trigger for eye development. They were able to measure these short bursts of ATP using ATP sensors specially developed by Professor Dale. This is the first time researchers have been able to see and measure bursts of ATP so early in the development of living creatures.

The genes that initiate and direct eye development are well known and are collectively termed the Eye Field Transcription Factors” (EFTFs). One of the mysteries of the field is how these genes get turned on in the correct location and at the correct time to initiate eye development. The Warwick research shows that this short burst of ATP followed by accumulation of ADP is a key signal for initiating expression of the EFTFs and hence the development of the eye.

The discovery of this surprising new signal that literally switches on eye development it is not restricted to frogs. Mutations to the E-NTPDase2 gene on the human 9th chromosome is already known to cause severe head and eye defects. This suggests that this newly discovered mechanism for triggering eye development applies across a wide range of species.

This new understanding of how eye development is triggered will greatly

assist researchers exploring stem cells connected to eye development and opens up an avenue of a research that could in just a few decades lead to the ability to produce an “eye in a dish”.

Source: University of Warwick