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TET1 protein helps prevent congenital defects and late-onset diseases

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In the earliest stages of embryonic development, a protein known as TET1 may be the factor that tips the balance toward health or disease. The first evidence for this vital role of TET1 is presented in *Nature Genetics* by researchers from KU Leuven (University of Leuven), Belgium. They found that TET1 is necessary to prevent congenital defects such as spina bifida as well as mental retardation and cancer later in life.

Every mammal starts off as a cluster of cells with the same genetic material. As the embryo develops, this DNA is used to generate the cell-specific building blocks for lungs, the brain, and every other tissue and organ in the body. To determine which genetic information is needed for a specific cell—and when—chemical marks or methyl groups are added to the DNA at specific positions. Erasing a mark often switches on a specific message, whereas adding a mark usually switches it off. This determines how proteins interpret the genetic information.

In 2009, a team of researchers at Harvard University demonstrated that the TET protein family erases marks from the DNA and is thus essential for the proper development of the embryo. The precise role of the three family members, however, remained a mystery.

Professor Kian Koh from the KU Leuven Department of Development and Regeneration, who was a co-lead author of the Harvard study, has now been able to shed light on the role of the first family member, TET1. He found that the protein plays a vital role in the embryonic stage

that precedes the development of individual organs.

"TET1 is the only TET protein found in detectable amounts at this stage," Professor Koh explains. "This suggests that it has a unique function. To find out which one, we created mice that lack TET1."

"The protein prevents the incorrect marking of DNA," Professor Koh continues. "We found that the loss of TET1 may lead to severe defects that cause the brain or spinal cord to develop outside the body. The causes of such defects, including spina bifida, are very complex, of course, but our findings suggest that TET1 plays a pivotal role in preventing them."

But incorrect marking of the DNA may also cause late-onset diseases. "This is because TET1 is necessary to control the speed of embryonic development. If the timing for the start of a specific stage is off, the foetus may die. And if it survives, the marks on the DNA may still be improperly erased, possibly leading to mental retardation and cancer later in life."

These findings open up new avenues of research into the origin and prevention of both congenital disorders and various late-onset diseases.

More information: Rita Khoueiry et al, Lineage-specific functions of TET1 in the postimplantation mouse embryo, *Nature Genetics* (2017). DOI: 10.1038/ng.3868

Provided by KU Leuven