

## Researchers Create Atlas of Transcription Factor Combinations

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**S** *tudy provides breakthrough blueprint for studying differentiation and evolution*

In a significant leap forward in the understanding of how specific types of tissue are determined to develop in mammals, an international team of scientists has succeeded in mapping the entire network of DNA-binding transcription factors and their interactions. This global network, indicating which factors can combine to determine cell fate, will be published in the March 5 issue of the journal *Cell*.

Transcription factors (TFs) are proteins that bind to specific DNA sequences in order to direct which genes should be turned on or off in a tissue. Tissue specificity – whether embryonic tissue develops into lungs or kidneys or skin, for example – is determined by how and which TFs bind to genes. Between 2,000 and 3,000 transcription factor proteins are encoded by the human genome, potentially creating more than 4 million potential protein pairings.



Trey Ideker, PhD

It has long been appreciated that different combinations of TFs are active in different tissues. But given the enormous number of TFs and potential pairings, it has been difficult to precisely identify which combinations are functional, according to principal investigator Trey Ideker, PhD, chief of the Division of Genetics at the University of California, San Diego, School of Medicine.

The integrated approach to systematically map all possible combinations of TFs in mammals has generated large data sets in both humans and mice. The complete network contains 762 human and 877 mouse interactions between TFs, indicating TF pairs that can work in combination.

“The availability of this large combinatorial network of transcription factors will provide scientists with many opportunities to study gene regulation, tissue differentiation and evolution in mammals,” said Ideker, professor in the Department of Medicine and at UCSD’s Jacobs School of Engineering. He added that analysis of the network shows that highly connected TFs are broadly expressed across tissues, and that roughly half of the interactions are conserved between mouse and human.

The researcher team identified nearly 1,000 different pairs of TF proteins that can be wired together, representing the blueprint of all possible combinations that direct gene expression in mammals. The work may provide researchers with the clues necessary to one day determine how stem cells can be reprogrammed into a particular organ or tissue type.

The research team comprised 41 scientists from 17 different institutions around the world led by UC San Diego, the RIKEN Institute in Japan, and King Abdullah University of Science and Technology in Saudi Arabia. Members of UC San Diego were supported by a grant from the National Institute of Mental Health. Researchers at the RIKEN Omics Science Center were supported by the Japanese Ministry of Education, Culture, Sports, Science and Technology.

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