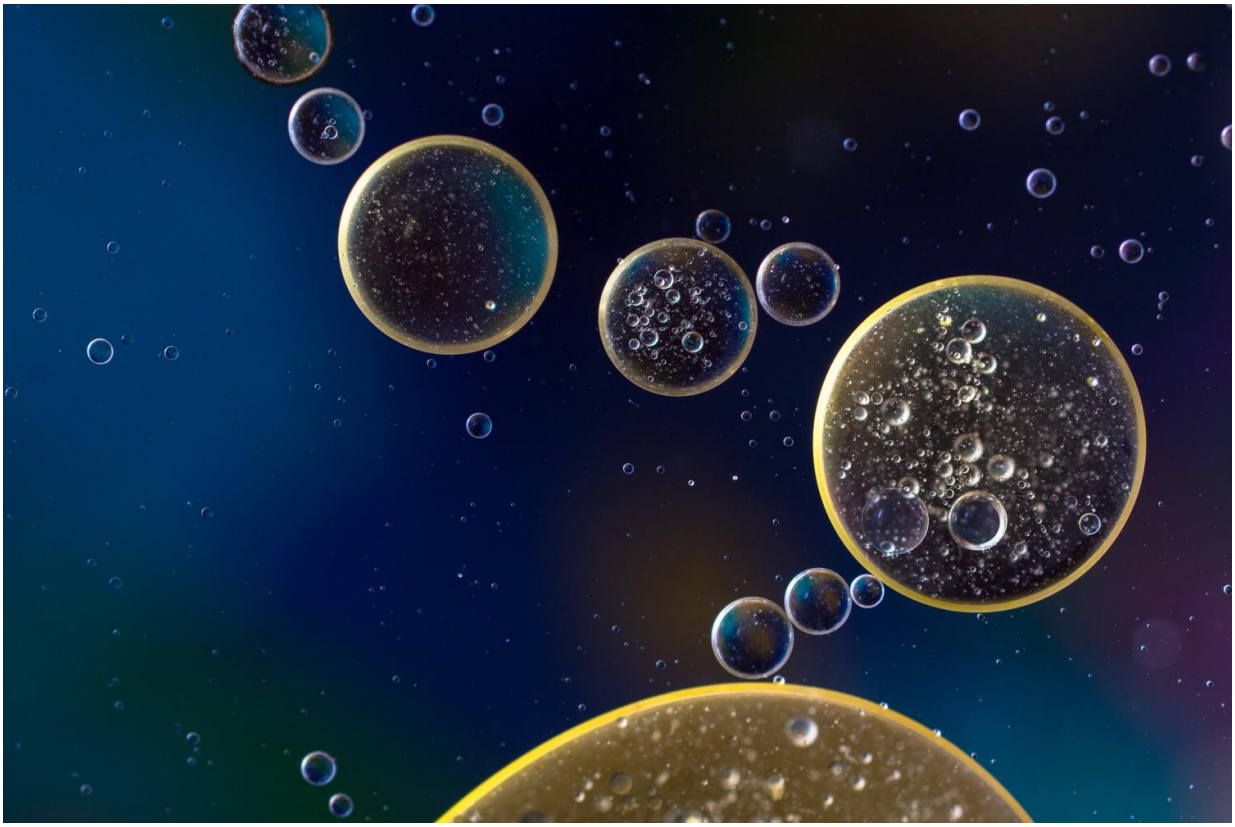
New discovery explains why cells with identical genes perform unique jobs

April 5 2018



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Scientists have made a significant discovery that explains how and why the billions of different cells in our bodies look and act so differently despite containing identical genes. The discovery, made by a team from

the Smurfit Institute of Genetics at Trinity College Dublin, applies to all complex animals, including humans.

The team has discovered a completely new family of proteins in animals with vertebrae—including fish, reptiles, birds and mammals—that they have named PALI1 and PALI2. Fascinatingly, these families of proteins both originated from genes that have gained new functions since vertebrate and invertebrate species evolved from one another millions of years ago. Specifically, PALI1 is vital for embryonic development and in particular for controlling cellular identity.

Associate Professor in Genetics at Trinity, Adrian Bracken, led the team that has just published the findings in the leading international scientific journal, *Molecular Cell*. Dr Eric Conway and Dr Emilia Jerman, the lead authors on the paper, previously worked as PhD students in the laboratory of Professor Bracken, while the team also collaborated with the Haruhiko Koseki lab at the Riken Institute in Japan.

The new work helps towards understanding why a blood cell and a brain cell look and act very differently yet contain exactly the same genes. This puzzling question about the so-called 'cellular identity' is central to the field of epigenetics, which strives to explain how cells in your body, with identical sets of genes, can look and behave so differently. The study of epigenetics has provided key molecular insights into how every type of cell has its own unique pattern of genes that are either switched on or off in a tightly controlled manner.

Central to this is a group of epigenetic regulators, called Polycombs, which are vital to regulating cellular identity in multicellular organisms of both the plant and animal kingdoms. The Bracken lab studies the biology of these Polycomb epigenetic regulators, and their newly discovered PALI1 and PALI2 proteins form a new family of Polycombs that are unique in that they are only present in vertebrates—they are not

found in invertebrate animals, or plants.

Commenting on the findings, Professor Bracken said: "This discovery of PALI1 and PALI2 is an important step forward in our understanding of how stem cells specialise in complex animals, such as fish, reptiles, birds and mammals."

"In addition to its relevance to stem cell biology and regenerative medicine, it may also have implications for future cancer therapies. For example, we are also studying a related Polycomb protein called EZH2, whose function is deregulated in certain blood and brain cancers. Several new drugs have been developed to target EZH2 to treat these patients, but our new results suggest these patients could also potentially be treated by drugs targeting the PALI1 and PALI2 Polycomb proteins, which might provide additional benefit."

"This ongoing research in the Bracken lab is supported by funding from the Irish Cancer Society, the Irish Research Council, Worldwide Cancer Research, the Health Research Board and Science Foundation Ireland, for which we are very grateful."

More information: *Molecular Cell* (2018). DOI: 10.1016/j.molcel.2018.03.005

Provided by Trinity College Dublin