Structure of key epigenetics component identified

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Scientists from the Structural Genomics Consortium (SGC) have determined the 3D structure of a key protein component involved in enabling "epigenetic code" to be copied accurately from cell to cell.

Epigenetic code is a series of chemical switches that is added onto our DNA in order to ensure that the cells in our body can form different types of tissue, for example liver and skin, despite having identical DNA genetic code.

When DNA is copied from cell to cell, it is essential that the epigenetic code is also copied accurately. If not, a liver cell may divide into another type of cell, such as a nerve or eye cell. A breakdown in this system might also mean that a gene for cell growth is accidentally switched on, for example, leading to unregulated cell growth and the development of tumours.

Research published in 2007 showed the importance of the nuclear protein UHRF1 in ensuring that the epigenetic code is accurately copied. Epigenetic switches are created by the addition of a chemical group (methyl) to DNA in a process known as methylation, facilitated by the enzyme DNMT1. The researchers believe that when this code is copied, UHRF1 ensures the accuracy of the process, like a proof-reader checks a typeset article before printing.

The key element of UHRF1 involved in this "proofreading" process is known as the Set and Ring Associated (SRA) domain, but the exact

mechanisms by which the SRA domain accomplishes this task were unclear. Today, in three different articles, the journal *Nature* publishes the structure of the key element of UHRF1 that facilitates this process.

"Given the increasing focus on epigenetics as a mechanism behind cancer, elucidating the structure of UHRF1 may provide crucial insights into what goes wrong," says Professor Sirano Dhe-Paganon from the Structural Genomics Consortium laboratories at the University of Toronto, Canada.

The structural papers not only represent an advance for the epigenetics field, but also an advance for how the science was done. The concurrent publication of the three papers highlights the competitive nature of this field, but in fact these papers were made possible because the SGC, in keeping with its policy of making its data freely and immediately available, made the underlying information available in the Protein Data Bank late in 2007. The availability of this information allowed the other groups to make more rapid progress in their own work.

"By releasing the structural information into the public databases as soon as it was available, we have ensured that other research groups could make immediate and maximum benefit from the shared knowledge," says Professor Dhe-Paganon.

Professor Masahiro Shirakawa from Kyoto University, Japan, openly acknowledges that the SGC data was crucial to his team's paper, which also appears in today's edition of Nature.

"We would like to express our gratitude to the researchers at the SGC for making their available on net," says Professor Shirakawa. "Structural biology is a complex, but very important field, with the potential to drive forward important research in many areas. The information provided by the SGC significantly speeded up our own work."

The SGC's "open source" policy contrasts with the accepted practice in the structural biology field, which is to make the underlying data available only after the work appears in print. However, Professor Al Edwards, Director of the SGC, believes strongly that data such as the 3D structure of proteins should be made freely available as soon as they are discovered.

"From the outset, it's been important to us to release our structural data immediately," says Professor Edwards. "This is contrary to the way many scientists work, but we believe it is crucial for facilitating scientific and medical progress, and our policy has not inhibited our ability to publish our work in the top journals. All the protein structures studied by the SGC have medical relevance and making them freely available ensures that scientists are able to use them to make progress in our understanding of disease and the development of new drugs."

Source: Wellcome Trust