New knowledge about the building blocks of life

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A study of an enzyme that helps build and repair DNA in living organisms increases our understanding of how these processes are controlled and how we can use this to combat infections.

Chemists at the Faculty of Science at Lund University in Sweden, together with their colleagues in Umeå and Stockholm, have studied the enzyme ribonucleotide reductase, (RNR). By using synchrotron radiation, including at MAX IV Laboratory in Lund, they are able to show the three-dimensional structure of the enzyme and the building blocks of DNA. They have thereby discovered how the building blocks bind to each other and how this is used to control the function of the enzyme.

The researchers believe that in the future, their results, which are currently at the level of basic research, can contribute to the development of new antibacterial drugs, including drugs that fight nosocomial infection, also known as hospital-acquired infection. The RNR enzyme that the researchers have studied derives from the bacterium pseudomonas aeruginosa, which is associated with nosocomial infections.

A challenge in the development of drugs against these pathogens is that their enzymes are often similar to ours. If you inhibit the foreign enzyme in order to kill the bacteria, there is always a risk that this will affect the person's own enzymes, which leads to side-effects or even toxicity.

"However, we have discovered that the binding of molecules differs greatly between the human enzyme and the bacteria's RNR enzyme, so the risk of side-effects is therefore considerably smaller", says Derek Logan, senior lecturer at the Faculty of Science in Lund.

In the study, the researchers also discovered that RNR from the type of bacteria that causes the sexually transmitted disease chlamydia has the same type of binding to the DNA building blocks. Therefore, Derek Logan does not rule out the possibility that, in the future, these new findings could lead to a new treatment of chlamydia. However, he predicts that applications in the form of development programs for new drugs are at least ten years into the future.

The research results have been presented in an article in the scientific journal *Structure*.

More information: Renzo Johansson et al, Structural Mechanism of Allosteric Activity Regulation in a Ribonucleotide Reductase with Double ATP Cones, *Structure* (2016). DOI: 10.1016/j.str.2016.03.025

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