

Danish scientists solve old blood mystery

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Scientists at the research centre MEMBRANES at Aarhus University, Denmark, have completed an old puzzle, which since the 60s from many sides has been regarded as impossible to complete. The challenge was to solve the structure of the protecting protein complex that forms when haemoglobin is released from red cells and becomes toxic. This toxic release of haemoglobin occurs in many diseases affecting red cell stability, e.g. malaria.

Technically, the most important finding in this report in *Nature* is a high-resolution three-dimensional mapping of the so-called 'haptoglobin-haemoglobin complex'.

"After many failing experiments, our breakthrough came when we gave up using human material and went to the local slaughterhouse to purchase pig blood. Not a particular high-technological approach, but this transition from studying human.blood to blood from a species with close homology had magic effects. After running into dead ends for two years and trying out the most complex gene-technological ways to produce the right material, it suddenly worked", says Søren Kragh Moestrup, the head of the research group at Department of Biomedicine.

The discovery provides new essential information on haemoglobin that makes up most of the red <u>cell interior</u>. Haemoglobin is an essential <u>blood</u> component for transport of oxygen, but it becomes toxic with potential damaging effects on tissues, in particular the kidneys, when it is released from the red cells. An excessive release can occur in many diseases, such as <u>malaria</u> and other infections.



However, the body has a sophisticated defence system. The first line defence is carried out by the <u>blood protein</u> haptoglobin, which captures haemoglobin and gates it to a receptor that engulfs the haemoglobin-haptoglobin complex. This function of the receptor named CD163 was originally discovered by the same group.

"We have now shown how this unique <u>protein</u> complex forms by generation of a detailed 3-dimensional map of each atom. This shows for the first time how the complex is formed and explains the tight protein association", says PhD Christian Brix Folsted Andersen. He has together with Master's student Morten Torvund-Jensen been an essential driving force in the project.

The results have also led to an unexpected discovery of a novel type of protein structure and a new patent submission on exploitation of the discovery for use in generation of a new type of synthetic proteins to be used in therapy and diagnostics.

More information: "Structure of the haptoglobin-haemoglobin complex", *Nature*.

Provided by Aarhus University

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