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A new avenue to better medicines

Selectively modifying hormones and using them as medicinal substances

German-American research team produces metal-peptide complexes

Researchers at the RUB and from Berkeley have used metal complexes to modify peptide hormones. In the Journal of the American Chemical Society, they report for the first time on the three-dimensional structure of the resulting metal-peptide compounds. "With this work, we have laid the molecular foundation for the development of better medicines" says Prof. Raphael Stoll from the Faculty of Chemistry and Biochemistry at the Ruhr-University. The team examined hormones that influence the sensation of pain and tumour growth.

Peptide hormones have many functions in the body

Hormones consisting of amino acids, the peptide hormones, convey bodily sensations such as pain and hunger, but also transmit growth signals. One example of this is insulin, which is important for the control of blood sugar levels. In interaction with specific receptors, the G-protein-coupled receptors, peptide hormones transport their messages to the cells. The hormones can be specifically chemically modified so that their effect changes, for example pain tolerance is lowered, or tumour growth inhibited. The German-Californian group of researchers has now found a new way to modify peptide hormones.

Metal complexes react with various peptide hormones

The first time they used a metal complex, namely, a rhodium compound, which reacts with the amino acid tyrosine. The precious metal rhodium is used as a catalyst in the synthesis of highly complex medicinal substances in the research laboratory as well as in industrial plants. Among other things, the researchers analysed the peptide hormone encephalin, which is important for the sensation of pain, and octreotide. The latter is a synthetic derivative of the growth hormone somatostatin, approved as a medicinal substance and already used in the treatment of certain tumours. The reaction with the metal complex was highly selective. Although the hormones consist of hundreds of atoms, the rhodium compound was always coordinated by the carbon ring of the tyrosine - the phenol ring.

Structure determined by NMR spectroscopy

The team also clarified the structure of the resulting metal-peptide complexes. "We hope to develop other metal-containing, peptide-like substances by building on these basic studies" says Prof. Dr. Nils-Metzler-Nolte of the Chair of Inorganic Chemistry I. "These could modulate the effect of naturally occurring peptide hormones and, for example, be used as a novel remedy for pain or cancer". For the project, the Californian colleagues made their knowledge of the special reactivity of the rhodium compound available. The researchers in Bochum contributed their experience with metal-peptides, the corresponding receptors and the structural analysis of biological macromolecules. "This again demonstrates that cutting-edge competitive research can only be carried out efficiently within a research association", says Prof. Stoll. The German Research Foundation (SFB 642 and Research Unit 630) and the Research Department for Interfacial Systems Chemistry at RUB supported the work.

Bibliographic record

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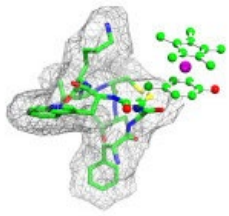
LINKS

- Medical inorganic chemistry at the RUB
- Biomolecular spectroscopy at the RUB



With NMR spectroscopy, the RUB research team determined the three-dimensional structure of the metal-peptide complexes. The metal atom, rhodium (magenta), binds to the peptides's amino acid tyrosine, more specifically to the phenol group – a circular structure consisting of six carbon atoms (green), one oxygen atom (red) and hydrogen atoms (not shown). The second circular carbon structure (green) above the rhodium atom represents a so called Cp* group. Via metal coordination, rhodium is bound between the two carbon rings. The gray net symbolizes the surface of the molecule.

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