

New drug to tackle fat problems

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Medical researchers at the University of Sheffield have defined the structure of a key part of the human obesity receptor- an essential factor in the regulation of body fat- which could help provide new treatments for the complications of obesity and anorexia.

This major advance in research, published in the journal *Structure*, will greatly enhance the ability to generate drugs which can both block and stimulate the receptor for the obesity <u>hormone leptin</u>. This could have life-changing effects on people suffering from the <u>complications of</u> <u>obesity</u> and malnutrition.

Researchers have solved the challenging <u>crystal structure</u> of the leptinbinding domain of the obesity receptor using state of the art X-ray crystallography, helping them to work out how to block or stimulate the receptor. Leptin, the obesity hormone, is produced by fat and excess leptin predisposes overweight people to conditions such as multiple sclerosis, cancer and heart disease whilst a deficiency in leptin, as occurs in malnutrition, results in infertility and immunodeficiency.

Blocking the receptor, and therefore the excessive actions of leptin, could prevent the complications of obesity and stimulating the receptor may improve fertility and the immune response.

Professor Richard Ross, Professor of Endocrinology at the University of Sheffield said: "This pioneering research gives us the potential to generate <u>new drugs</u> that could treat conditions and diseases associated with obesity such as Multiple Sclerosis, diabetes and cardiovascular



disease.

"Modulating the actions of the obesity receptor provides a novel approach to the treatment of conditions associated with both obesity and anorexia and has the potential to make a massive difference to millions of people whose quality of life and health is hindered by obesity or malnutrition."

Controlling appetite is a fundamental basic physiological drive which in turn is connected to many other aspects of physiology, in particular fertility and the immune response.

Professor Pete Artymiuk, from the University of Sheffield's Department of Molecular Biology and Biotechnology, said: "The <u>human obesity</u> receptor binds the hormone leptin and together they play a key role in regulating appetite, fertility, and immunity.

"Using X-ray crystallography we have solved the structure of the leptinbinding domain of the receptor bound to a potential therapeutic antibody that blocks leptin binding. This is the first crystal structure for any part of this important receptor.

"Because we now know the precise atomic structure of the receptor we can begin to design drug molecules that can alter its activity. This can be useful in the treatment of a variety of diseases ranging from obesity to autoimmune diseases including multiple sclerosis."

Provided by University of Sheffield

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