

## PRESS RELEASE

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### **A new path for the future generation of glucose-measuring biosensors**

- *CIC bioGUNE researchers have proven the close connection between proteins that were thought to be completely independent and isolated*
- *This discovery could lead to new glucose measurement methods in blood, which is essential to control diabetes, a chronic disease which affects more than 300 million people worldwide*
- *Current techniques measure glucose concentration in blood, but other more reliable sensors are being researched, based on other fluids such as urine, for example*

(Bilbao, 2013-01-03).- CIC bioGUNE researchers have opened a new path for the future development of biosensors that enable glucose measurement in the blood and also in other fluids that are thought to be more effective, such as urine. For this, a complex scientific process has been developed in which a prevailing paradigm in the scientific community concerning the binding and communication mechanisms between proteins was questioned.

Subcellular communication mechanisms are based on the interaction between proteins, or between proteins and metabolites and other ligands. These phenomena help to explain most of the protein functions in living organisms, but in order to do so it is essential that each protein knows exactly to which ligand it must be bound.

Until now, the scientific community widely believed that there was a double binding mechanism between proteins, which was differentiated and isolated like two independent process: some proteins were bound just with one mechanism called “induced fit” (the protein takes the form of the ligand during the association process), while other proteins were bound exclusively with the so called “conformational selection” mechanism (like a lock that needs a key with defined characteristics, the binding process between a protein and a ligand will take place insofar as its shapes enable said fit).

This project, however, led by Dr Óscar Millet, from the Structural Biology Unit at CIC bioGUNE and published in the November issue of the Journal of the American Chemical Society, refutes this paradigm and states that slight modifications introduced with genetic engineering in the hinge regions between two proteins are enough to alter the actual binding mechanism.

To develop this study, two bacterial periplasmic binding proteins were taken as models. These proteins are bound with a spectacular conformational change (closing two domains round a hinge region) which is similar to the process that carnivorous plants use to trap insects between their fleshy lobes.

“The main result of our work is proving that both mechanisms are intimately connected and that we can go from one to another just by introducing small modifications in the protein,” explains Óscar Millet.

“Not only have we understood this mechanism, but we have seen that the difference between this induced fit and the conformational selection is very subtle; they are actually not two independent processes – everything is connected. Nature is always subtle, and small variations to the chemical composition of the hinge lead us from one mechanism to the other,” added the CIC bioGUNE researcher.

“This mechanism is completely governed by the hinge region to the point that by exchanging the hinges using genetic engineering, the change of mechanism also happens: the GGBP with the RBP hinge acts with induced fit and vice versa, the RBP with the GGBP hinge binds to the substratum with lock-and-key mechanism,” Millet declares.

“By understanding the mechanism by which periplasmic proteins trap glucose to insert it into the cells, these molecules could be used as biosensors”, explains Millet. Thanks to these biosensors, glucose concentration could be measured in fluids other than blood, for example urine. This would make the process easier and would provide more reliable data than traditional glucose concentration measurement methods in the blood of diabetes patients.

The techniques that are used today can only give an approximate measurement of blood glucose concentration, as there are other substances that hide it. Any advance, therefore, in the search for new diagnosis methods will improve the control of the disease.

## **Diabetes**

It is very important for diabetes patients to measure their glucose concentration, as diabetes is a serious chronic disorder that affects more than 300 million people worldwide, and 5 million in Spain. This metabolic disease is caused by low production of a hormone – insulin – in the pancreas or when the body does not use this hormone properly. Insulin is involved in the transport of glucose to the interior of the cells, which turn it into useful energy.

In diabetics, the low generation of insulin or inadequate usage in the body leads to an excessive blood glucose concentration and causes many symptoms such as tiredness, weight loss, neuropathies, sight problems and in extreme cases, death.

### **References for the study**

Carbohydrate Affinity for the Glucose–Galactose Binding Protein Is Regulated by Allosteric Domain Motions

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