Press Release

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How proteins find their way out of cells*, an essential mechanism for cellular function*

The **Institute of Molecular Biology and Biotechnology (IMBB) of FoRTH** participates in the effort to understand a fundamental biological problem, namely how cells regulate trafficking of their proteins. Some of the research results are presented in today's edition of Nature, one of the most authoritative international scientific journals. They stem from intercontinental cooperation between the research teams Tassos Economou, IMBB researcher and Associate Professor at the Biology Department of the University of Crete and that of Charalambos Kalodimou, Associate Professor at Rutgers University (New Jersey, USA).

Thousands of proteins are produced inside our cells. More than a third of these proteins can fulfill their function only after migrating to the outside of the cell, becoming anchored to the cell membrane or target specific subcellular compartments. These processes are essential for life. Examples of migrating proteins are insulin (whose absence leads to diabetes), antibodies (that combat infections), membrane channels (essential amongst other fro neuronal cell function) and toxin-proteins secreted by pathogenic microorganisms.

How do migrant proteins find the way to their final destinations and how do they go through cell membranes? More than 30 years ago, Gunter Blobel (Rockefeller University, New York) discovered that migrating proteins contain chemical signals called signal peptides and was awarded the Nobel prize of 1999 for this finding. These signal peptides have a double function: they act like postal addresses as well as like miniscule handles. Depending on its final cellular destination, each migrating protein bears a different address. In 2007 the Economou/Kalodimos labs revealed how signal peptides bind to a specific cellular receptor on the membrane. This recognition results in traping of migrating proteins on the membrane surface. How the channel subsequently opens was unknown. With the new publication in Nature the Economou/Kalodimos teams reveal an essential, previously unknown role of signal-peptides. Specifically, the researchers show that as soon as the signal peptide binds to its docking groove it acts as a key that opens the secretory channel thus allowing the remaining part of the migrant protein to cross the membrane through the channel.

The discovery of this key biological mechanism is expected to help improve our understanding of the tens of diseases that are caused by defective signal peptides on secretory proteins. Such diseases include coronary heart disease, lymphocytic leukemia, and malfunctioning of endocrine glands. In addition, it offers the possibility to optimize the biotechnological production of human biopharmaceuticals using microbial cell-factories. The pursuit of these research directions as well as the further exploration of subcellular protein trafficking at IMBB is funded by European and American grants, the General Secretariat of Research and Technology and american and european companies.

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