EURYI Awards 2004

Press Information

Dr. Alexey RAK

– Physical Biochemistry –

Project:

Rab proteins & their partners: towards a comprehensive structural model of the role of the GTPases in vesicular transport.

Rab proteins represent the largest branch of the Ras superfamily of small GTPases, with at least 60 Rab proteins identified in the human genome. Rab GTPases are central and multifunctional regulators of vesicular membrane transport controlling both the exo- and endocytic pathways. Rab proteins are believed to determine the specificity of docking and fusion of intracellular compartments by functioning as signals for assembly of macromolecular machinery controlling those events. Mutations in the Rab GTPases or interacting proteins have been implicated in a number of human diseases, ranging from immunologycal disorders to blindness. Moreover, in a number of vascular, lung, and thyroid diseases as well as in some cancer forms the over-expression of several Rab GTPases is observed and correlates with the disease progression.
The aim of the presented proposal is to use a combination of biochemical and biophysical approaches to assemble a comprehensive model for the structural basis of RabGTPase interaction with other proteins throughout their functional cycle. As the primary method, we choose protein X-ray crystallography, which is in most cases the only method that can provide detailed information about structure of macromolecular complexes on the atomic level. We propose to crystallize and solve the structures of a range of complexes between RabGTPases and their interacting proteins to reveal the molecular basis of their molecular selectivity. In addition to purely academic interest in understanding the mechanistic principles of central functional units of eukaryotic cells, this work is expected to lead to practical applications in the treatment of Rab associated diseases.
The project will demonstrate an example of the combination of targeted elucidation of the role of GTPases in vesicular transport and efficient high throughput approaches in molecular biology, biochemistry, crystallization and protein structure determination.

Comments:

The project is a frontal attack to solve all relevant structures of Rab complexes. An important, competitive project in a competitive field, where the candidate has shown himself already a world leader.

Alexey Rak is an excellent young scientist with a brilliant publication record and outstanding scientific perspective. With the EURYI award he would stay in his favorite institute in Dortmund and turn down the offers from US universities/institutes.

Very complex and original crystallographic project with a biological question. The project is organized in a straightforward way. The planned programme is ambitious, but the candidate seems to be the right person to accomplish it. His background in biochemistry is very strong, giving him expertise in protein expression and, equally important, in the design and interpretation of relevant assay systems.

The Dortmund Institute is arguably the best place in Europe for these studies.

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