EURYI Awards 2004

Press Information

Dr. Bas van STEENSEL

– Biology –

Project:

Whole genome analysis of the regulation of chromatin structure and gene expression

One of the greatest challenges in modern biology is to understand how cellular programs of gene expression are established and maintained. The packaging of DNA into chromatin is an important mechanism of gene regulation. Several proteins, such as chromatin remodeling factors, linker histones, HMG proteins, and heterochromatin proteins are believed to control the gene expression by modulating this packaging. However, the mechanisms of action of these proteins and their intricate network of combinatorial interactions in the living cell are poorly understood. Here, a systematic "in vivo chromatin genomics" approach is proposed to reveal the roles and functions of proteins that control chromatin structure. In particular, the mechanisms of action of these proteins in the regulation of gene expression will be dissected. Several in vivo whole-genome approaches will be integrated, using the fruit fly Drosophila melanogaster as a model system. We will perform systematic mapping of in vivo binding sites for a large set of representative proteins involved in the regulation of chromatin structure, using a whole-genome assay developed by the applicant. Furthermore, new techniques will be developed for genome-wide mapping of structural features of chromatin.
The resulting global maps of protein binding and chromatin structure will cover the entire fly genome at a resolution of ~2kb. These maps will be complemented by whole-genome studies of gene regulation, employing RNAi and genetic techniques. Finally, all data will integrated and modeled using state-of-the-art bioinformatics methods. This project will provide a wealth of new insights into the principles of gene regulation by chromatin in vivo, in the natural context of the entire genome. In addition, the resulting large database of genomic maps of protein binding, chromatin structure, and gene expression will be an important resource to the research community.

Comments:

The project is important for whole genome mapping of the function and localization of chromatin interaction proteins.

Bas van Steensel has an excellent track record. He identified the protein (TRF2) that protects human telomeres from erosion while working with Titia de Lange at the Rockefeller University, and went on to develop a very effective and completely original method for mapping the position of DNA-binding proteins with Steve Henikoff in Seattle, based on a tethered DNA methylating enzyme. He has already undertaken a lot of unique, important, and very good work. He already leads a group of 8 and has a tenured position. With the award he would stay in Amsterdam at the Netherlands Cancer Institute.

Excellent project. Van Steensel is now exploiting his 'DamID' method to explore the location of a large number of DNA-binding proteins. There is a nice balance of practical work, and descriptive analysis together with sophisticated bioinformatics approaches that promise to shed considerable light on patterns of gene expression (and their control) in higher eukaryotes.

The Netherlands Cancer Centre is a much admired beacon of excellence in Europe, and provides a perfect supportive and stimulating environment for this type of work.

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