EURYI Awards 2004

Press Information

Dr. Zsuzsanna IZSVAK

– Molecular Biology –

Project:

***Sleeping Beauty* transposition: biology and application in vertebrates**

Transposons are mobile genetic elements that are ubiquitous in nature, and make up significant fractions of genomes. Active transposons that move via a DNA intermediate (as opposed to retroelements) are essentially missing in vertebrate species, due to their mutational inactivation over evolutionary time. I was involved in resurrecting an ancient fish transposon called Sleeping Beauty (SB), which efficiently transposes in a wide range of vertebrate cells, including humans. SB is a unique experimental tool to address questions related to the mechanism of transpositional DNA recombination, as well as the intricate molecular interactions between the transposon and the host cell. In addition, SB opened up new possibilities for the development of transposon-based genetic/genomic technologies in vertebrates. After the basic characterization of the new transposon, I investigated DNA-protein interactions, regulation of complex assembly and target site selection during transposition. My other focus was to identify cellular mechanisms influencing transposition, including DNA repair. I began to explore SB's potential as a tool in gene discovery and molecular therapy. The proposed project builds upon my previous work, expanding in the following directions. First, my research is aimed at surveying different cellular factors involved in DNA replication, repair, damage-signalling and cell-cycle regulation for their potential roles in establishing a successful transposition event. Second, I propose to manipulate the transposon to generate hyperactive mutants by in vitro evolution for enhanced utility as an insertional mutagen in vertebrate models such as fish and mice. I further plan to manipulate SB's target site selection in order to achieve targeted transposition into predetermined loci, or chromosomal regions, in human cells for safe gene therapy. The proposed research will extend our understanding of the principal molecular processes involved in cellular responses to DNA transposition, and contribute to the development of safe and efficient molecular tools for genetic manipulations in vertebrates.

Comments:

Transposons make up a surprisingly large fraction of human DNA. The successful targeting of transposons would open promising new possibilities for gene therapy.

Excellent candidate with outstanding publication record. She is already a leader in the field and is ready to lead a bigger group.

The excellent proposal is based on an original idea of the candidate. It brings transposon mutagenesis in vertebrates to another level and has a high potential for biomedical applications as well as for basic research, especially in developmental genetics. The approach competes with other novel methods of gene activation. Scientifically very important. There are strong competitors in Japan and the US. The award would ensure her competitiveness, give her the chance to carry out the big work programme in all aspects and keep her scientific capacity in Europe.

This award would guarantee her independence and assure the stability of the team she has formed with her husband in Europe for the next five years.

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