UNIVERSITE D'EVRY
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GENETHON

Advanced methods for industrial production, purification and characterisation of gene vectors

June 14th-26th, 2004 - Evry University, Genopole®-EVRY, France

CERTIFICATE of ATTENDANCE

Hereby, I certify that **Dr Mohammad Mahdi GHAHRAMANI SENO**, from University of London (UK), attended the Conference and Practical Course: **Advanced methods for industrial production, purification and characterisation of gene vectors** held in Evry from June, 14th to 26th, 2004.

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Poster n°27

Evry-Fr. 2004

THE USE OF SIRNA TECHNOLOGY FOR THE IDENTIFICATION OF DIFFERENTIALLY EXPRESSED GENES IN DUCHENNE MUSCULAR DYSTROPY: POSSIBLE TARGETS FOR GENE THERAPY

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Deuchenne Muscular Dystrophy (DMD) is a fatal progressive muscle wasting and the most common inheritable genetic disease affecting one of each 3500 male birth. Molecular pathology of DMD and animal models like mdx mice which is primarily initiated with the absence of dystrophin in myofibers is very extensively studied, but little understood because of multiple interactions that dystrophin has established with many other cellular, transmembrane and extracellular proteins like Dystrophin associated proteins (DAP). Proteins which form part of the DAP have also been found to be mutated in other inherited forms of muscular dystrophy like limb girdle muscular dystrophy.

The applications of gene therapy protocols for DMD still present many daunting challenges which is partly due to intrinsic features of the dystrophin gene. Hence, improvement of the understanding of the underlying primary molecular pathology leading to DMD might pave the way for the discovery of new starting points.

Here we present an approach to use RNAi technology to study the events occurring in muscle cell development due to dystrophin deficiency. siRNA has been proven to be a powerful technology to study molecular effects due to a knock down of singular genes.

A time course study approach on two dystrophic mice models and their normal counterparts showed indicated the status of dystrophin and three other DAP i.e. utrophin, β-dystroglycan and β-sarcoglycan in primary cultures. Then an established siRNA against Zyxin, a protein involved in focal adhesion, was used to optimize conditions in myogenic cell line C2C12. We have also validated four strong siRNAs active against dystrophin in primary cultures. Next step is devising vectors expressing siRNA against dystrophin to use in vitro and in vivo to study expression profiling in the absence/ step by step disappearance of dystrophin. This will hopefully lead us to new useful therapeutic targets.