British Society for Gene Therapy

ATTENDANCE CERTIFICATE

This is to certify that M. M. Ghahramani Seno attended the 2nd annual meeting of the British Society for Gene Therapy 3-5 April 2005 at Hulme Hall Manchester.

Professor Leonard W Seymour, President of the British Society for Gene Therapy

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The use of siRNA technology to identify differentially expressed genes in Duchenne Muscular Dystropy: possible targets for gene therapy

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Duchenne Muscular Dystrophy (DMD) is one of a group of genetically heterogeneous muscular dystrophies that are characterized by progressive weakness and wasting of skeletal muscle. Loss of myofibres occurs in response to a deficiency of dystrophin, a protein which is believed to be responsible for myofibre maintenance and integrity. Dystrophin forms a link between the cytoskeleton and the membrane-spanning dystrophin-associated glycoprotein complex (DAPC), indicative of a structural role for dystrophin.

The application of gene therapy protocols for DMD still presents many daunting challenges due partly to intrinsic features of the dystrophin gene. Hence, improvement in the understanding of the underlying primary molecular events leading to a dystrophic pathology might pave the way for the discovery of new starting points.

Here we present a strategy to use RNAi technology to study the events occurring in muscle cell development due to dystrophin deficiency. RNAi has been proven to be a powerful technology to study molecular effects due to knockdown of single genes. We have used a series of siRNAs to target and knock down the expression of dystrophin in primary cultures of mouse muscle, and subsequently used transcriptomic array analysis to identify genes whose expression was affected in response to dystrophin deficiency. The data obtained from this experiment, which include some very interesting potential new targets, are currently being analysed. We are also developing a recombinant adeno-associated virus (rAAV) vector expressing an shRNA targeting dystrophin. The use of such rAAV-shDNA vectors will enable us to target dystrophin in vivo to obtain a better and potentially curative insight into the pathophysiology of DMD.