IRCE 2005

**13th Multi-Disciplinary Iranian Researchers Conference in Europe**

**Leeds University, UK July 2nd 2005**

This is to certify that

***"Dr Mohammad Mahdi Ghahramani Seno"***

has actively participated and presented a paper in "Molecular Medicine & Genetics" entitled

***"Potent Dystrophin Knock-Down In Vitro And In Vivo Using Rnai Technonlogy And Expression Signature Of Myotubes With Dystrophin Knocked Down: Attempts At Unravelling The Mystery"***

at 13th Multi-disciplinary Iranian Researchers Conference at Leeds University, UK on July 2, 2005.

Maziar Asefi
*Conference co-chair*

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*Conference co-chair*

Iranian Journal of Public Health, Vol 34, No Sup (2005)

# Potent Dystrophin knock-Down in Vitro and in Vivo Using RNAi Technonlogy and Expression Signature of Myotubes with Dystrophin knocked Down: Attempts at Unravelling the Mystery

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## Abstract

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 were 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 have also developed a recombinant adeno-associated virus (rAAV) vector expressing an shRNA targeting dystrophin. The use of such rAAV-shDNA vectors enables us to target dystrophin in vivo to obtain a better and potentially curative insight into the pathophysiology of DMD.