

HUMAN MUSCLE CELLS AS A MODEL TO STUDY THE EXPRESSION AND PHYSIOLOGICAL ROLE OF THE NRE ENZYME

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The objective of our study was to investigate neuropathy target esterase-related enzyme (NRE; PNPLA7) expression and its functional characteristics in human muscle cells as a model organism for insulin-targeted tissues. More specifically, our previous preliminary studies confirmed the presence of this unexplored enzyme in both myoblasts and myotubes and indicated a role for NRE in the energy metabolism. The human NRE enzyme is predicted to be around 146 kDa. Though the crystal structure of NRE has not yet been defined, gene sequence analysis and homology modelling predict the presence of N-terminal single-pass transmembrane domain, three cyclic nucleotide binding sites, possible glycosylation sites and C-terminal patatin-like catalytic domain. Furthermore, analysis also predicts the existence of several isomers some of which do not have a catalytic domain or in other words, possibly lack esterase/lipase functions. Sequence alignment reveals that NRE is conserved through rat, mice and human species. High NTE homology with more investigated enzyme NTE or PNPLA6 suggests that NRE might also be a target of organophosphorus compounds (OP) which implies NRE involvement in OP caused pathological conditions including poorly defined intermediate-myopathy syndrome. Therefore, by following changes in NRE mRNA, the protein and activity level in cells exposed to different stimuli mimicking real life conditions, we tried to define NRE's physiological role and its potential to be used as a new therapeutic target in OP poisoning or in wider research. The enzyme was cloned, expressed and studied as the esterase in kinetic experiments *in vitro* following interactions with potential substrate and inhibitor. In this way, we also evaluated its enzymatic properties. Since little is known about this enzyme's physiological role and biological relevance, any findings would most certainly contribute to the understanding of the importance of NRE, which still calls for a detailed clarification.