**Statin-induced mytotoxicity**

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Statins are amongst the most widely used drugs throughout the world with up to 30% of the population taking one of the statins on a regular basis. Their success can be attributed to excellent efficacy in reducing cholesterol levels, and in long-term clinical studies, statins have been shown to reduce cardiovascular morbidity and mortality. However, a significant proportion of patients complain of muscle pains which can result in drug discontinuation. In most cases, this is mild and is not associated with a rise in creatinine phosphokinase (CPK) levels. Causality can be difficult to attribute in such cases. In the most severe cases, statins can cause rhabdomyolysis which can lead to death – a high frequency of such adverse events resulted in the withdrawal of cerivastatin. There has been increasing interest in the role of genetic factors in predisposing to statin myotoxicity. To date, only the *SLCO1B1 c.521T>C* (rs4149056) polymorphism has been shown to be important at a genome wide level (and largely for simvastatin). This correlates with the known effect of SLCO1B1 on the pharmacokinetics of statins. Further work is currently on-going using next generation sequencing technologies, the preliminary results of which will be presented in the lecture. It is also of course important to consider non-genetic predisposing factors – the most important of these are inhibitory drug interactions which lead to an increase in statin exposure. While it is clear that increased exposure which can be due to either genetic or environmental factors can predispose to statin myotoxicity, much less is known about the pharmacodynamic factors predisposing to statin myotoxicity. These issues will be discussed in the lecture.