INTRODUCTION

In a recent review of the literature for appropriate animal models to study the efficacy of statins, Pecoraro, et al stated that “Given the complexity of cardiovascular diseases and its multifactorial nature, it is unlikely that a single model will perfectly represent human physiology…” [3]. The main difficulty with the use of mice for the study of statins is that they lack the plasma cholesteryl ester transfer protein that facilitates the transport of cholesteryl esters and triglycerides between lipoproteins. Therefore, mice are not the best model of atherogenesis in humans. However, these authors also suggest the use of Apo E-/- transgenic mice in studies to model severe dyslipidemia [3]. When fed a lipid-enriched diet, the total cholesterol in Apo E-/- knockout mice can reach five times the level in wild-type C57BL/6J mice, and statins have been shown to significantly reduce the total cholesterol [4]. In addition, studies in Apo E-/- mice have shown the antiatherosclerotic effect of statins through a anti-inflammatory mechanism on heart vessels in addition to their cholesterol-lowering activity [4,5].

We propose to evaluate the immune response following vaccination in Apo E-/- transgenic mice undergoing statin treatment. An initial study will determine the therapeutic window for statin treatment of transgenic mice fed a lipid-enriched diet. From the literature this window is expected to be from 21-28 days. That therapeutic window will be used for evaluation of the immune response following vaccination in mice undergoing statin treatment. An initial study will determine the therapeutic window for statin treatment of mice fed a lipid-enriched diet. From the literature this window is expected to be between 21-28 days. That therapeutic window will be used for evaluation of the innate immune response following vaccination in mice undergoing statin treatment.