Background
Atopic dermatitis is a skin disorder which affects 5-20% of the population in the Western countries. Treatment is largely confined to the application of anti-inflammatory drugs, such as corticosteroids and calcineurin inhibitors. Because such treatments show transient effects and do not mediate long-lasting effects, there is a great need of drugs that interfere with initial triggers of the disease. Appropriate animal models are essential for the identification of potential drugs. Here, we describe a model of atopic dermatitis that develops spontaneously in mice transgenic for human apolipoprotein C1 (APOC1).

Materials and methods
• Human APOC1 transgenic mice were developed as described previously (Jong et al., J Clin Invest 101, 145-152, 1998) to study the effects of its overexpression on lipoprotein metabolism. For the study of atopic dermatitis a breeding colony was established employing female APOC1 +/- and male APOC1 +/- mice.
• Measurements of epidermal hyperplasia and the enumeration of eosinophils and neutrophils were performed after staining of fixed tissue sections (5 µm) with hematoxyllin/eosin/saffran. Numbers of mast cells were assessed after toluidin blue staining.
• CD4+ or IgE+ cells were studied by the staining of cryosections with anti-CD4-biotin or anti-IgE-biotin, followed by incubation with HRP-labeled streptavidin, and using AEC as a substrate.
• Transepidermal water loss was measured with the use of a TM210 TEWAmeter.
• Pruritus measurements were performed for individual mice employing a Laboras system. Movements with a frequency between 5 and 25 Hz and a duration of at least 0.2 sec were found to reflect a scratch event.

Results
• Homozygous APOC1 +/- mice gradually develop symptoms of dermatitis evident from increased scaling, papules, lichenification and excoriations (Figure 1). Progression of disease is associated with spongiosis (not shown). APOC1 +/- mice remain free of symptoms (data not shown).
• Histopathology of the lesions reveals both epidermal and dermal hyperplasia (Figure 2) with an early involvement of eosinophils, mast cells and CD4+ T cells. At early age eosinophils outweigh the number of neutrophils; however, the latter increase in numbers and become more prominent at later age (Figure 3).

Figure 3 shows a gradual increase in numbers of mast cells when the mice grow older (open symbols reflect APOC1 +/- and wildtype mice).
• Importantly, APOC1 +/- mice have increased serum IgE levels from an age of 10 weeks onwards and subsequently show IgE+ mast cells in the dermis (Figures 2 and 4).
• Development of atopic dermatitis may be the consequence of a disturbed skin barrier as measured by increased transepidermal water loss (Figure 5).
• Atopic dermatitis in APOC1 +/- mice is associated with the development of pruritus (Figure 6).
• Inflammation and epidermal hyperplasia are suppressed by corticosteroid treatment (Figure 7).

Conclusions
• APOC1 +/- mice develop atopic dermatitis; various features are suggestive for a Th2-mediated mechanism, i.e. the involvement of eosinophils, mast cells and IgE.
• Symptoms of atopic dermatitis develop gradually and are associated with increased pruritus.
• APOC1 +/- mice have increased transepidermal water loss, which can already be detected at an age of 6 weeks; possibly, this enables the activation of the immune system by a trigger which favors a Th2-mediated mechanism.
• Various aspects of atopic dermatitis are sensitive to triamcinolone-acetonide; in addition, topical application of fluticasone or tacrolimus and oral administration of dexamethasone were found to suppress symptoms of atopic dermatitis in this model (data not shown).