1 Table of Abbreviations

2 Introduction
  2.1 Heat shock proteins
  2.2 The innate and the adaptive immune response to hsp
  2.3 Lymphocytes
  2.4 T cell receptor signaling
  2.5 T cell autoimmunity
  2.6 The T cell clone UZ3/4
  2.7 Inflammatory bowel disease
  2.8 TCR transgenic mice

3 Aims of the study

4 Materials
  4.1 Apparatus
  4.2 Software
  4.3 Chemicals, enzymes and kits
  4.4 Organisms
  4.5 Mammalian cell lines
  4.6 Mice
  4.7 Media and Buffers
  4.8 Antibodies
  4.9 Plasmids
  4.10 Oligonucleotides
# Methods

## 5.1 Molecular biological methods

5.1.1 *E. coli* heat shock transformation

5.1.2 Electroporation of *E. coli*

5.1.3 Polymerase chain reaction (PCR)

5.1.4 Southern Blot

5.1.5 RT-PCR

## 5.2 Cell culture and transfection

Electroporation of cultured cells

5.2.2 Retroviral Transduction

## 5.3 Biochemical methods

5.3.1 Western Blot

5.3.2 Pulse-chase metabolic labeling and immunoprecipitation.

## 5.4 Generation of transgenic mice

5.4.1 Cloning strategies for TCR expression constucts

5.4.2 Preparation of transgenic vector samples

5.4.3 Pronucleus injection of transgenic vector samples into fertilized eggs

5.4.4 Screening of potential transgenic founders

## 5.5 Animal procedures

5.5.1 BCG infection

5.5.2 Peptide immunization

5.5.3 Heterozygous breeding

## 5.6 Immunological methods

5.6.1 Flow Cytometry and Cell Sorting

5.6.2 Generation of MHC class I tetramers and staining of cells with tetramers

5.6.3 Cr-release assay

5.6.4 Cell isolation from different tissues

5.6.5 CD69 upregulation assay

## 5.7 Histology.
# Results

6.1 Expression of two TCR alpha chains in the CD8+ T cell clone UZ3/4

6.2 Surface expression of the TCR $\alpha_8$ chain but not the TCR $\alpha_7$ chain

6.3 Promiscuous peptide recognition of mycobacterial and murine peptides by the $\alpha_8/\beta_8$ TCR combination

6.4 Generation of TCR $\alpha_8$ and TCR $\beta_8$ transgenic mice

6.5 Peripheral TCR $\alpha_8$ and $\beta_8$ double transgenic mice are specific for the peptide SALQNAASIA from mycobacterial hsp60

6.6 Induction of CD8+ T cells specific for SALQNAASIA mycobacterial hsp60 peptide during mycobacterial infection

Generation of TCR $\alpha_7$ transgenic mice

Augmented levels of CD4+ TCR $\alpha^-\beta^+$ T cells in $\alpha_7.2$ mice

6.9 CD4+ TCR $\alpha^-\beta^+$ T cells show an activated phenotype

Accelerated course of IBD in $\alpha_7.2$ mice

6.11 Stabilization of endogenous TCR $\beta$ chains by non-pairing TCR $\alpha_7.2$

# Discussion

7.1 Promiscuous peptide recognition of a single TCR combination is responsible for the induction of autoimmune pathology

7.2 Hsp60 specific TCR transgenic mice

7.3 TCR $\nu_\alpha 7$ chain transgenic mice

7.4 Concluding remarks and outlook: