ApoSec tackles CNS
- EAE and Spinal Cord Injury -

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Background

• Multiple Sclerosis
  – Incidence: 149/100,000
  – USA: 250,000 – 350,000 patients
  – AUT: 12,000 patients
  – F:M = 2:1
  – 50 % need walking assistance within 15 years

Pathophysiology

- Autoimmune disease
- Initiating factors largely unknown
  - Genetic polymorphisms
  - Infections
  - Smoking i.a.
- Progressive loss of Myelin sheaths followed by astrocytic scars
- Relative preservation of Axons

Clinical Features

• Neurologic deficits due to loss of Myelin sheath and neurodegeneration in CNS
• Vast amount of different symptoms
• Onset abrupt or insidious
• Relapsing-remitting vs. Primary progressive
• Diagnosis: Clinical criteria, CSF, MRI

Neuron 52, 61-76 (2006)
EAE

• Experimental Autoimmune Encephalitis

• Common animal model for studying MS

• CD 4+ T-cell mediated disease (TH1 and TH17)

Allergol Int 57, 115-120 (2008)
TKI Bern

Prof. Britta Engelhardt
Setting

• 8-12 weeks old female C57/Bl6 mice

• Active immunisation with Myelin Oligodendrocyte Glycoprotein (MOG)
Group 1: d10: ApoSec (10x10^6) i.p.
Group 2: d10: Medium i.p.
Endpoint: d21
Evaluation

• Weight

• Clinical Score
  – 0: healthy
  – 0.5: limp tail
  – 1: hindleg weakness, unsteady gait
  – 2: hindleg paraplegia
  – 3: hindleg paraplegia, incontinence and loss of lower body control -> abort criterion
Evaluation

• Histology
  – H & E
  – Klüver-Barrera
  – CD3-staining
  – MAC-3-staining

• ELISA - sytemic cytokines

• Behavioural experiments?
Spinal Cord Injury
Epidemiology

- 50 per 1 million annually
- Most patients male, between 20 and 40 years
- 50% completely lack motory or sensory function below level of lesion
- 2/3 injury in cervical region

- Treatment of SCI: US$ 9.7 billion every year
- Costs often exceed US$ 1 million/patient

Pathophysiology

• Initial trauma
  – Contusion
  – Compression
  – Stretch injury

• Second hit
  – Ischemia
  – Inflammation
  – Edema formation
  – Further destruction of Axons

NeuroRx 1, 80-100 (2004)
Setting

- Male Sprague-dawley rats
- Laminectomy Th11
- Contusion trauma
- Infinite Horizon impactor device
Experiment

• Group 1: ApoSec (10x10^6) i.p. 40 min after trauma

• Group 2: Medium i.p. 40 min after trauma

• Group 3: NaCl i.p. 40 min after trauma

• Group 4: Sham control
Evaluation

• Clinical score (BBB-Score)

• Histology
  – H & E
  – Klüver-Barrera
  – MAC-3-staining

• ELISA – systemic/CSF cytokines

• MRI

• Behaviourial assessment (?)
Thank you for your attention!