

ApoSec tackles CNS

- *EAE and Spinal Cord Injury* -

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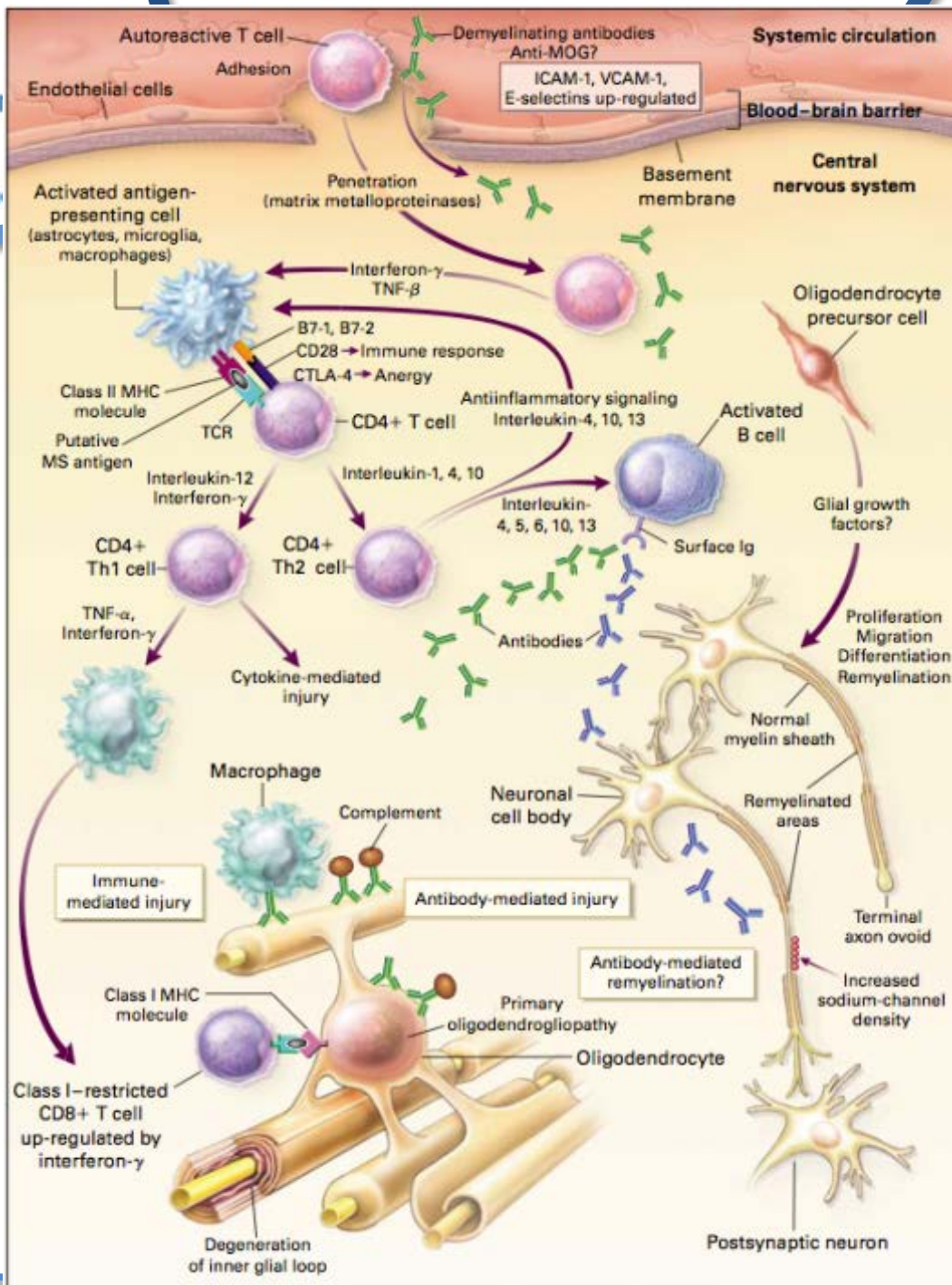
Background

- 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

N Engl J Med **343**, 938-952 (2000)

Pathophysiology

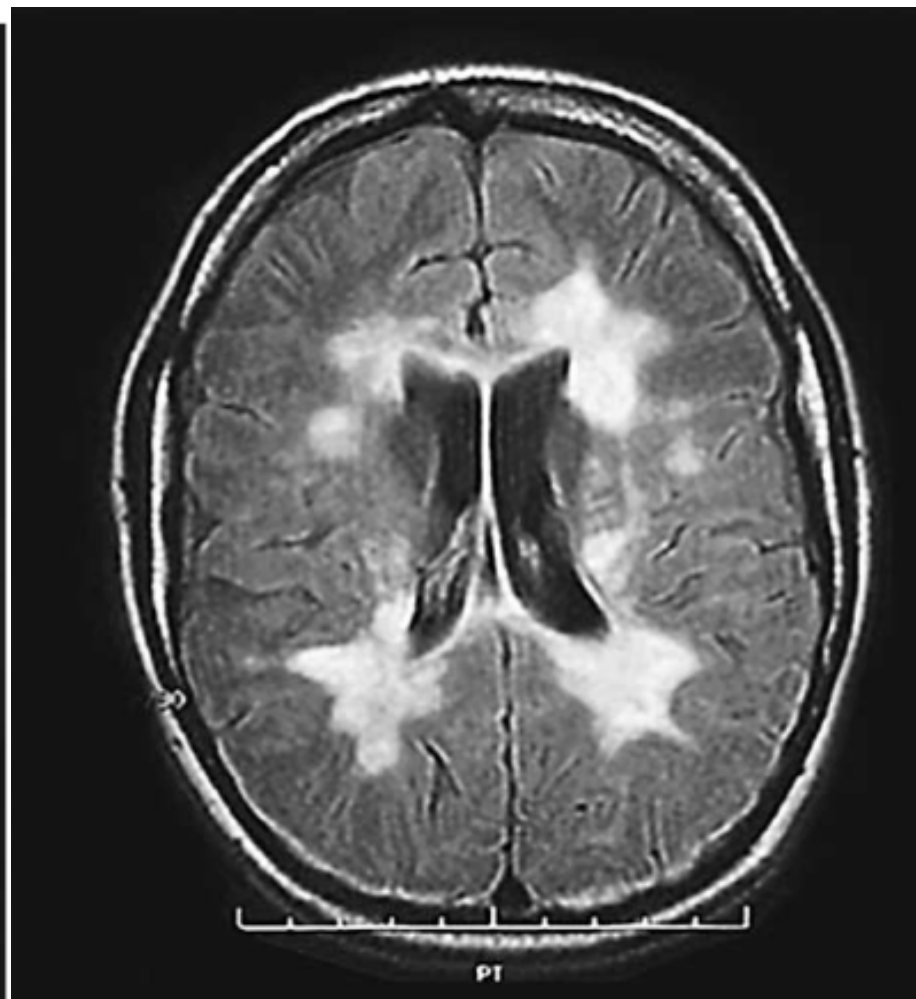
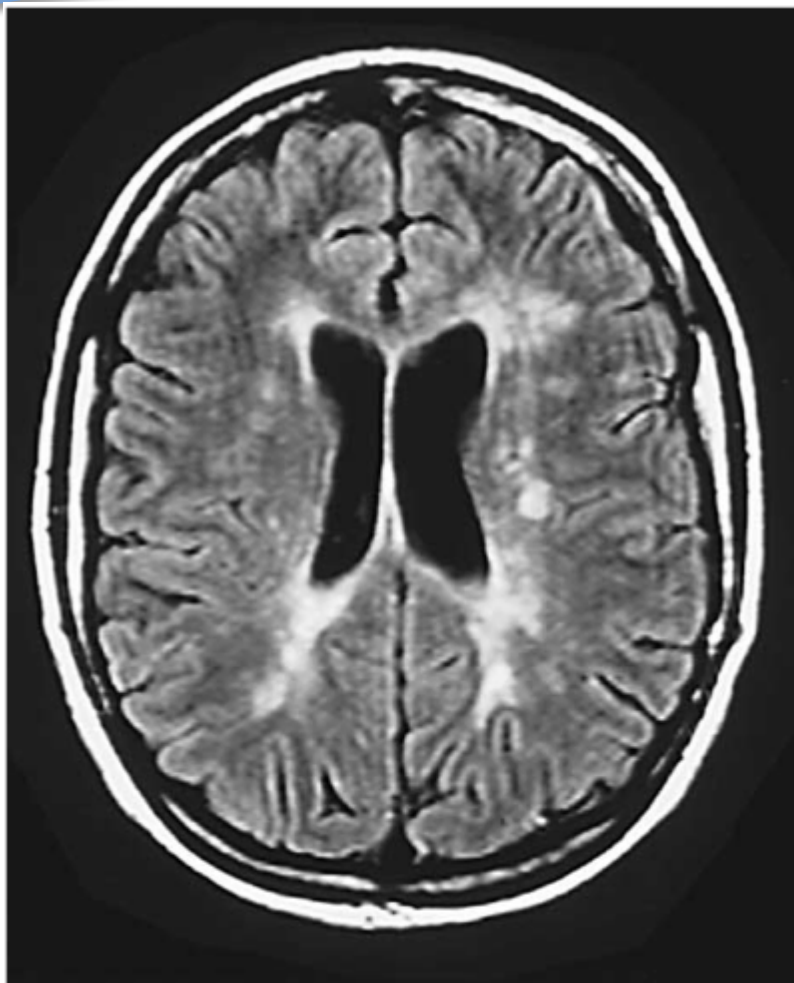
- Autoimmune disease
- Initiating factors largely unknown
 - Genetic polymorphisms
 - Infections
 - Smoking i.a.
- Progressive loss of Myelin sheaths followed by astrocytic scars
- Relative preservation of Axons



N Engl J Med 343, 938-952 (2000)

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



N Engl J Med 343, 938-952 (2000)

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)

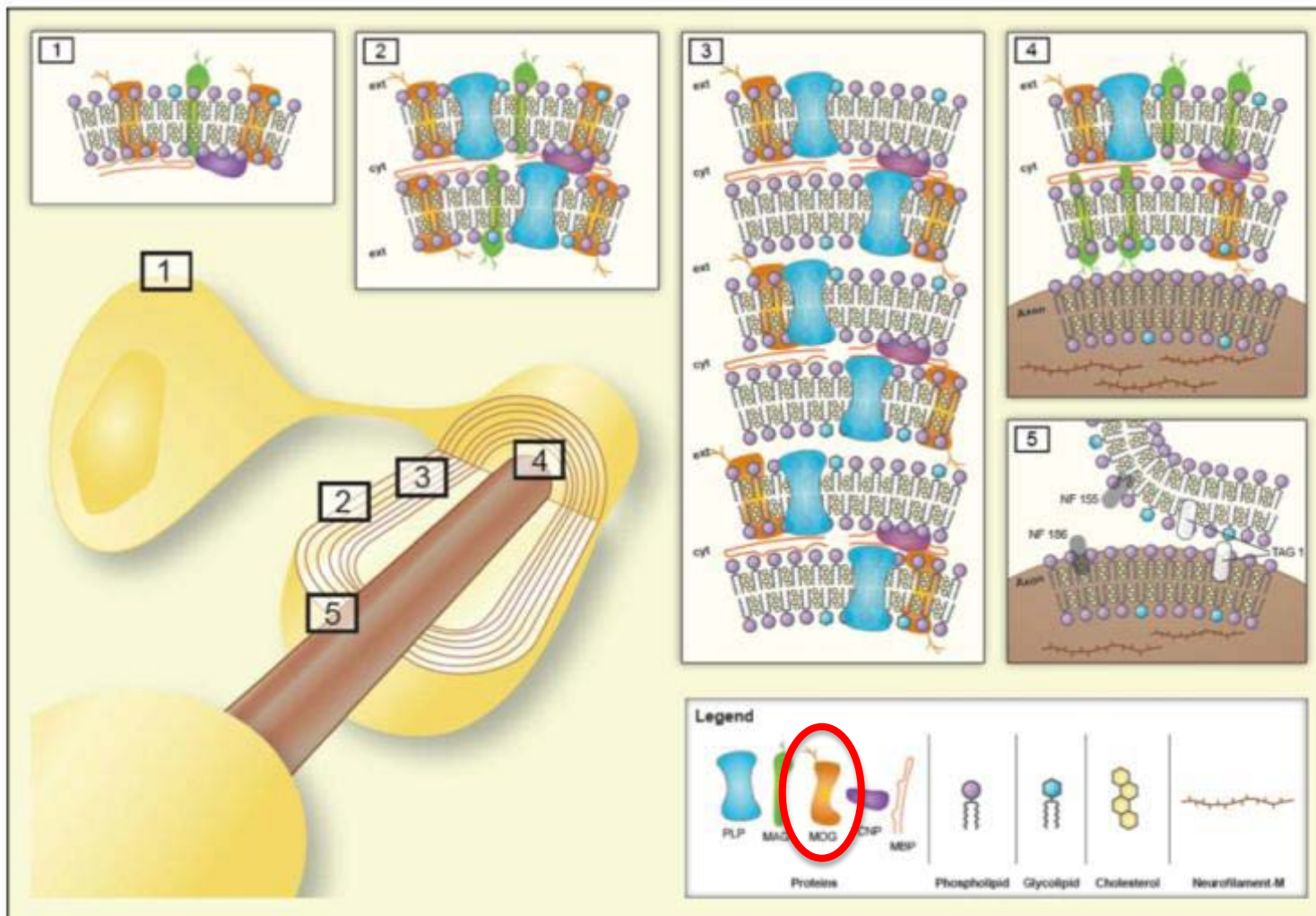
TKI Bern

Prof. Britta Engelhardt



Setting

- 8-12 weeks old female C57/Bl6 mice
- Active immunisation with Myelin Oligodendrocyte Glycoprotein (MOG)



d0 MOG
immunization

d1 PTX i.p.

d3 PTX i.p.

d10-d15

Clinical onset

Group 1: d10: ApoSec (10×10^6) i.p.

Group 2: d10: Medium i.p.

Group 3: d10: NaCl i.p.

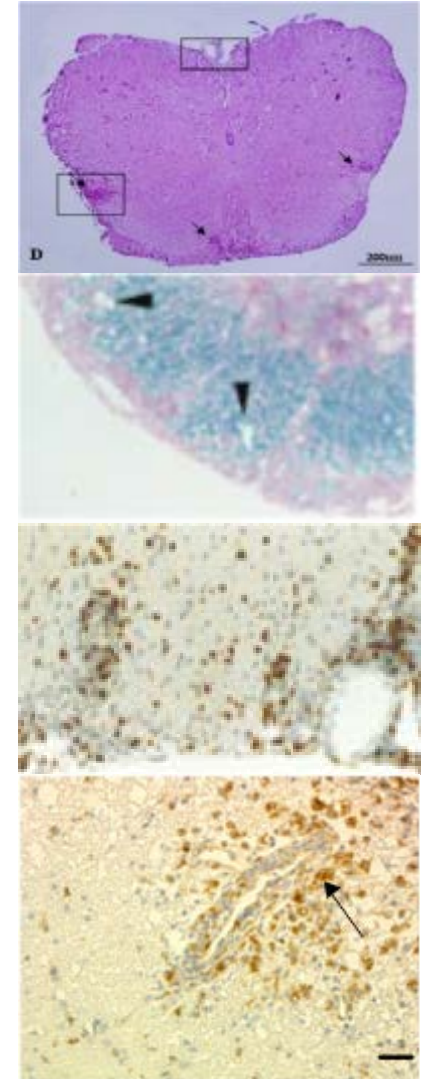
Endpoint: d21

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 - systemic cytokines
- Behaviourial 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

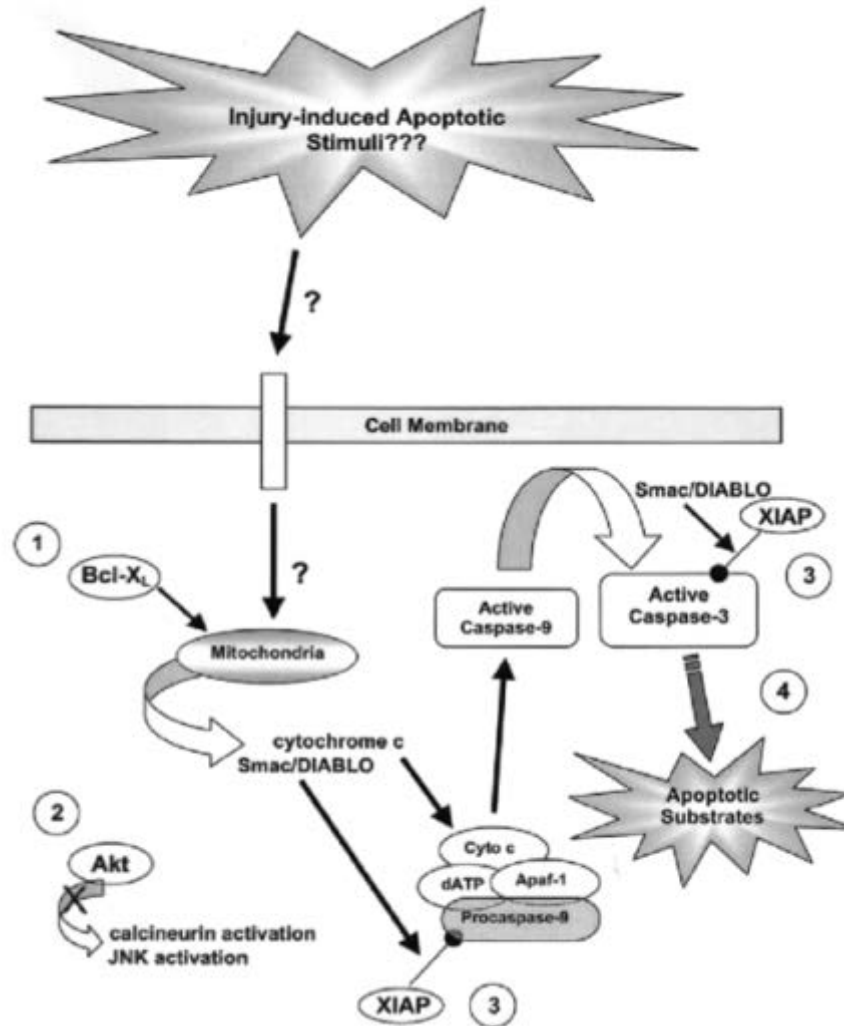
J Neurosurg **75**, 15-26 (1991)

J Neurotrauma **21**, 1355-1370 (2004)

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 (10×10^6) 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!