

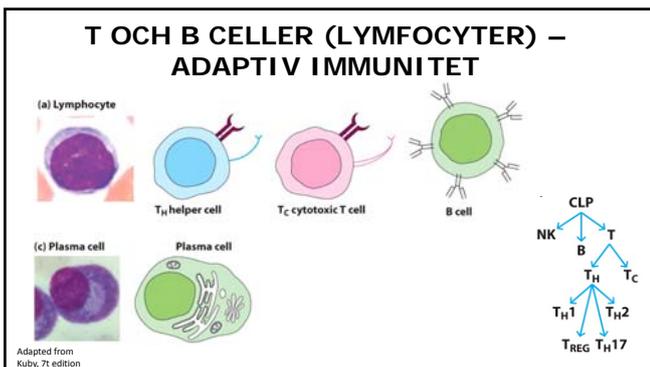
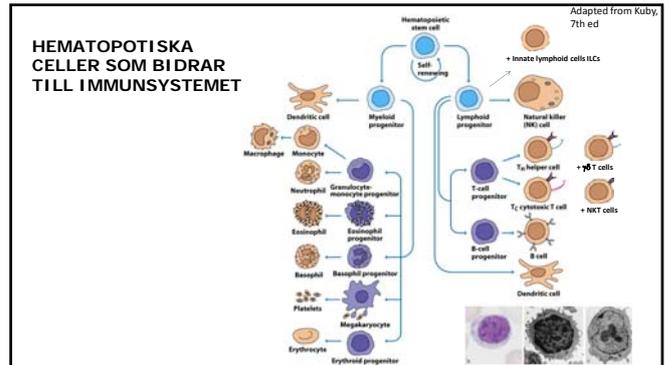
BASAL IMMUNOLOGI UR NEUROLOGISKT PERSPEKTIV

2018-05-24

Kristina Lejon, PhD
Docent
Klinisk Mikrobiologi/Infektion&Immunologi
Vicedekan, Utbildning Medicinska fakulteten

UMEÅ UNIVERSITET





AUTOIMMUN SJUKDOM = AVSAKNAD AV IMMUNOLOGISK TOLERANS

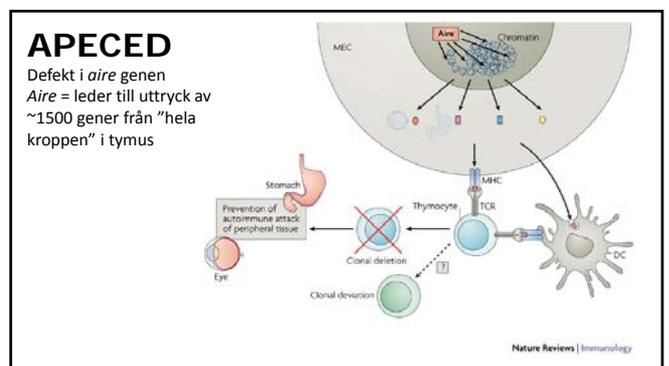
- Undermålig **selektion** mot autoreaktiva T- och B-celler i tymus och/eller benmärg
- Undermålig **perifer reglering** av autoreaktiva kloner med hjälp av Tregs och Bregs



APECED

(Autoimmune polyendocrinopathy candidiasis ectodermal dystrophy)

- Sällsynt monogen autoimmun sjukdom
- I Finland 1:25 000
- Många autoimmuna attacker
 - Typ 1 diabetes
 - Vitiligo
 - Addisons sjukdom
 - ...mm....

PROBLEM APECED

Normal AIRE expression: Thymus (Normal AIRE expression) → Deletion of self-reactive T cells → Protective immunity.

APECED: Thymus (Absence of AIRE) → Survival of self-reactive T cells → Autoimmunity.

Legend:
 ● Naive T cell
 ● Autoreactive T cell
 ● Regulatory T cell
 ● AIRE
 ● CD27
 ● CD27L

KOPPLING HLA ALLELER-AUTOIMMUNA SJUKDOMAR

- Vad som kan presenteras i tymus = selektion
- Vad som kan presenteras i periferin = immunsvär

Adapted from K 7th ed

B CELLS URVAL (SELEKTIONEN) I BENMÄRGEN

50-75% av alla B celler som bildas i benmärgen är autoreaktiva

Method: single cell cloning and assay

IHC: Hep-2 reactivity

ELISA: ssDNA, dsDNA, insulin, LPS

Group	CD54+	CD19+	CD10+	IgM+
Early immat.	+	+	+	+
Immat.	+	+	+	+
New emigrant	+	+	+	+
Mature naive	-	-	-	-

Meffre Wardemann 2008 Current Opinion in Immunology

FEL I URVALET FRÅN BENMÄRGEN TILL PERIFERIN?

B % of Hep-2 reactive B cell clones: Controls (n=11), MS (n=7), T1D (n=8), RA (n=10). P < 0.0001.

C % of polyreactive B cell clones: Controls (n=11), MS (n=7), T1D (n=8), RA (n=10). P = 0.0004.

D % of B cell clones reactive to whole nuclear extract: Controls (n=6), MS (n=7). P = 0.0298.

E % of antinuclear B cell clones: Controls (n=6), MS (n=7), T1D (n=8), RA (n=10), ND. P = 0.0286.

Ja!
För T1D, RA & MS!

Meffre JCI 2013

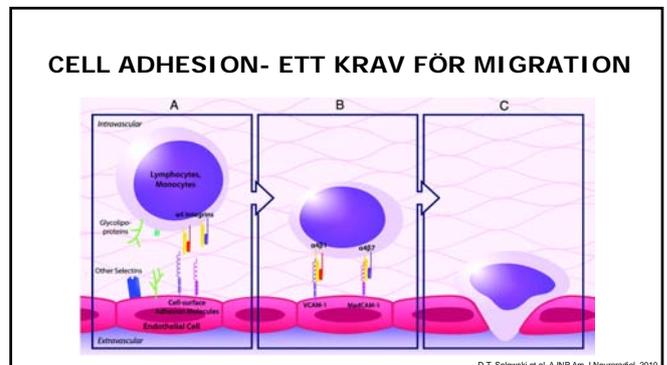
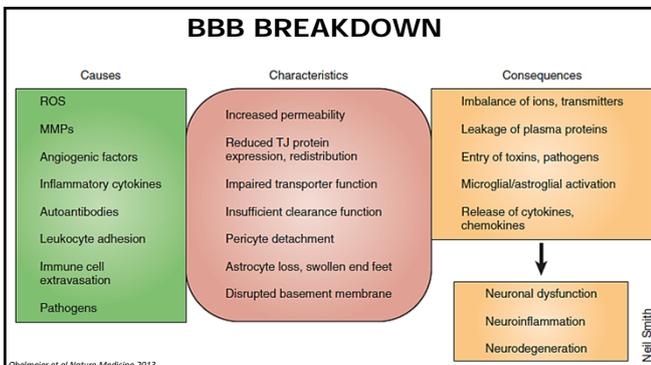
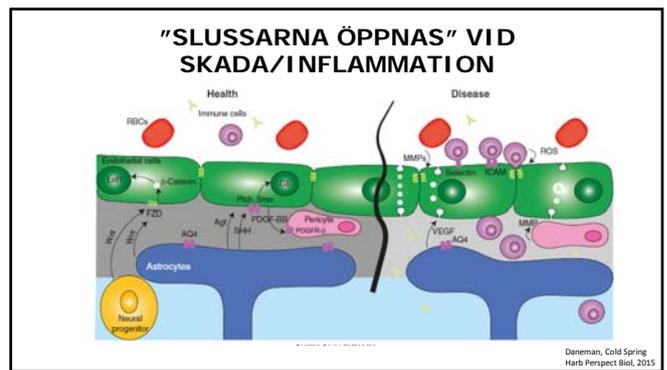
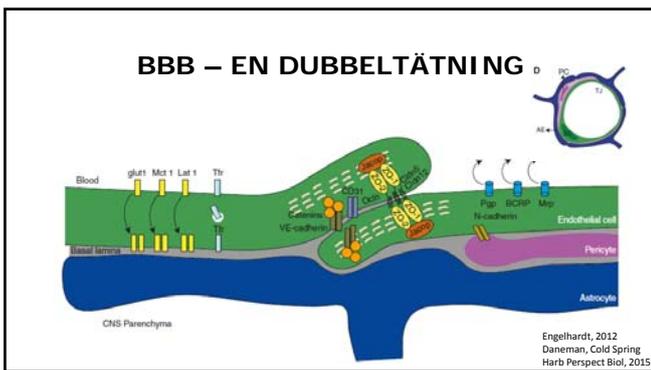
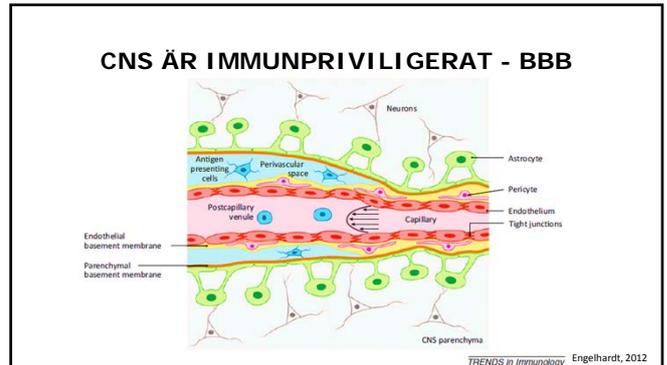
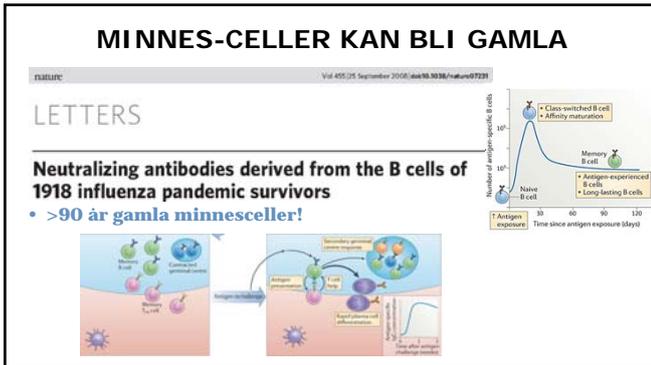
INITIERING AV ETT T-CELLS BEROENDE B-CELLS SVAR

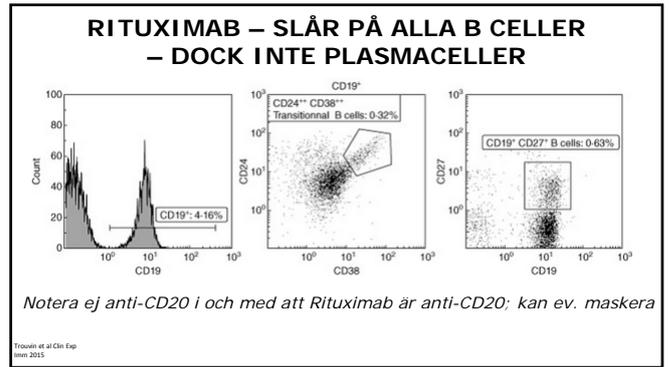
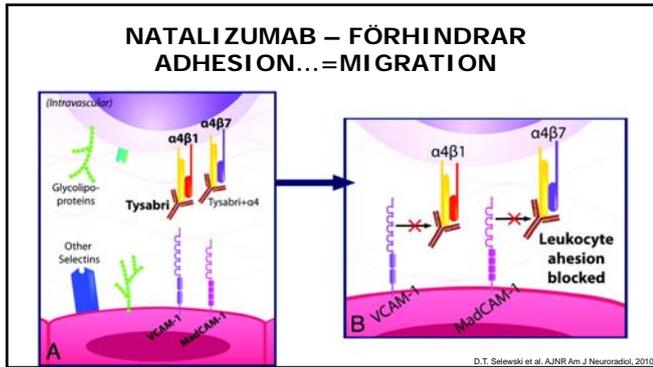
Adapted from Nat Rev Imm

ÖVERLEVAND AV PLASMACELLER

Långlivande plasma celler - återfinns i benmärgen - tas hand om av flera celltyper

Adapted from Kuby, 7th ed





Notera ej anti-CD20 i och med att Rituximab är anti-CD20; kan ev. maskera

RITUXIMAB BEHANDLING - UTSLAGNING AV B_{REGS}?

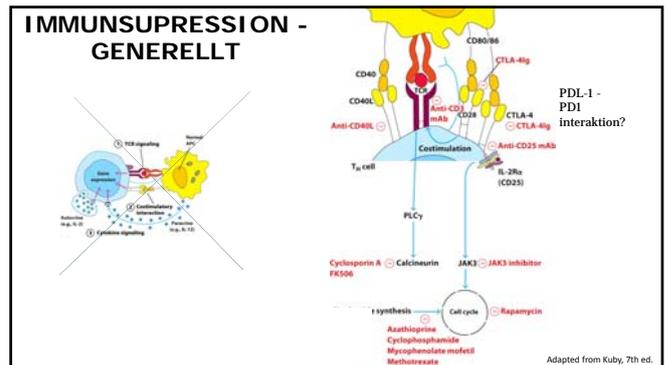
Development of Psoriasis After B Cell Depletion With Rituximab

Shoenk & Dan, Edward M. Vitai, and Paul Ilievsky

ARTHRITIS & RHEUMATISM
Vol. 50, No. 6, August 2008, pp 2715-2718
DOI 10.1002/art.23081
© 2007, American College of Rheumatology

RA patient (52-y old), no effect anti-TNF - Rituximab treatment, development of psoriasis after second round of treatment

SLE patient (26-y old), severe SLE, Rituximab treatment, development of psoriasis



Angel of the West, Julian Voss-Andrea

Tack för att du lyssnade!

Frågor? At your service!

UMEÅ UNIVERSITET