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2


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PUMA
THE GREAT


Does TAp73 show premature aging?


Regulation of mast cell proteases by serpinB1
in mast cell homeostasis and function
BACKGROUND
HYPOTHESIS

WIPI dependent non-canonical autophagy operating in neutrophil differentiation of APL cells

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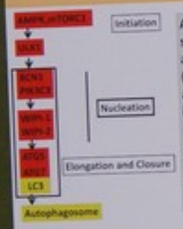
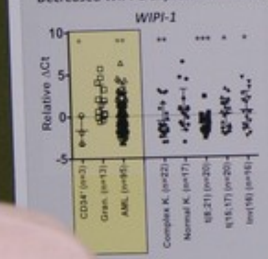
Introduction



Acute promyelocytic leukemia (APL) is characterized by a block in neutrophil
stage. Autophagy was recently shown to be associated with neutrophil diff
aggregated oncofusion protein PML-RARA in an APL cell line. Our studie
(ATRA)-induced neutrophil differentiation of APL cells is Beclin1-inde
autophagy mechanism referred to as myeloid differentiation-associated a
is Beclin 1-independent but dependent on the Phosphatidylinositol 3-kina
investigating the involvement of the phosphatidylinositol 3-phosphate P
acute myeloid leukemia (AML). WD-repeat proteins interacting with pho
activity and WIPI-1 as well as WIPI-2 are aberrantly expressed in a var
known regarding their role in myeloid leukemia.

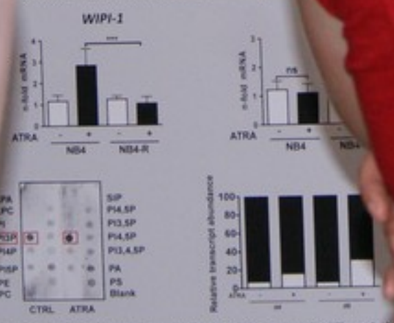
Results

1 Decreased WIPI-1 expression in AML patient samples



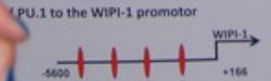
ed a 4-fold decrease of WIPI-1 expression in prima
d to granulocytes (n=14) from healthy donors. In c
only downregultated in particular AML subtypes.

not WIPI-2 levels increase upon neutrophil

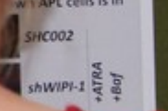


WIPI-1 but not WIPI-2 transcript level increase upon neutrophil differentiatio
ch more expressed in NB4 cells. Increased WIPI-PI3P binding upo

PU.1 to the WIPI-1 promotor



4 Attenuated
part due



APL cells is in

RTG 1331

Universität Konstanz

Role of LRH-1 in T cell development and function

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AIM OF STUDY

llenge...

vn about the expression and function of LRH-1 in T cells

racterize LRH-1 expression in different T cell subsets,
ction during lymphocyte development und effector
d out whether and how this transcription factor affects
s. Therefore, we generated conditional knockout mice
pecifically in T cells. I am also interested to find out
pathways regulate LRH-1 expression using cell culture

METHODS & RESULTS

LRH-1 is expressed in mature and immature

WT

RNA extraction

(A) LRH-1 mRNA expression in various organs
(B) LRH-1 expression in sorted thymocyte or spleen cell subsets (CD4+ and CD8+)

Conditional deletion of

WT or cKO
(CD4 promoter controlled, LRH-1$^{loxP/loxP}$;CD4-Cre$^{tg/wt}$)

C Number of T cells

CD8+

nd CD8+ T cell
spleen

LRH-1 plays a role in the re

WT or cKO

α-CD3

^{3}H-thymidine incorporation

stimulation with α-CD3

stimulation with PMA/Iono

OUTLOOK

Future plans...

My key question is why the deletion of L
numbers of mature T cells. Underlyin
apoptosis sensitivity or defects in
preliminary results, which support the
whether and how LRH-1 expression is
furthermore interested to investi
responses to antigens and viral infe

ating the conditional knockout mice and her

Group for funding

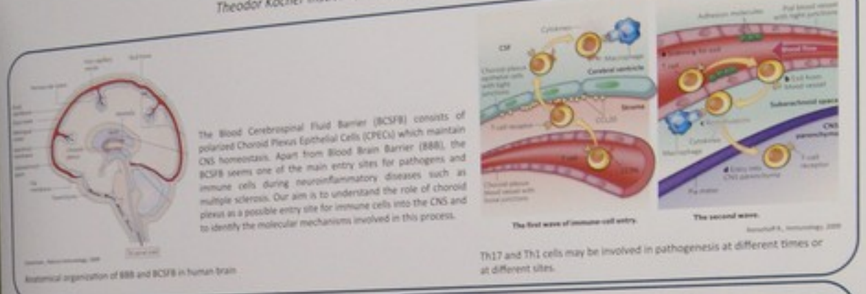
or their support

T cell trafficking across the blood cerebrospinal fluid barrier

Ivana Lazarevic, Henriette Schneider, Britta Engelhardt

Theodor Kocher Institute, University of Bern, Switzerland

UNIVERSITÄT BERN



Anatomical organization of BBB and BCSFB in human brain

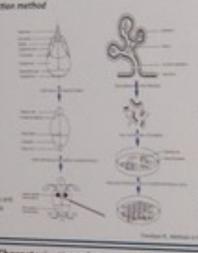
The Blood Cerebrospinal Fluid Barrier (BCSFB) consists of polarized Choroid Plexus Epithelial Cells (CPECs) which maintain CNS homeostasis. Apart from Blood Brain Barrier (BBB), the BCSFB seems one of the main entry sites for pathogens and immune cells during neuroinflammatory diseases such as multiple sclerosis. Our aim is to understand the role of choroid plexus as a possible entry site for immune cells into the CNS and to identify the molecular mechanisms involved in this process.

The first wave of immune-cell entry. The second wave.

Th17 and Th1 cells may be involved in pathogenesis at different times or at different sites.

Establishment of primary choroid plexus epithelial cell cultures

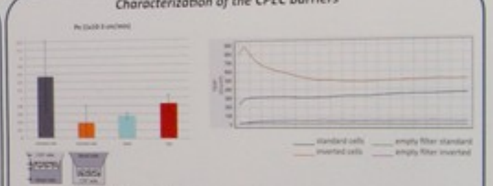
Mouse CP dissection method



Enzymatic and mechanical dissagregation of the tissue

Highly pure confluent CPEC monolayers suitable for studies addressing those functions in vitro.

Characterization of the CPEC barriers



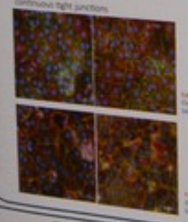
Barrier functions of inverted culture cells and standard culture cells: permeability measurement and transepithelial electrical resistance (TEER) measurement of the monolayers. EpiM and CSG as comparison.

Characterisation of primary CPEC cultures

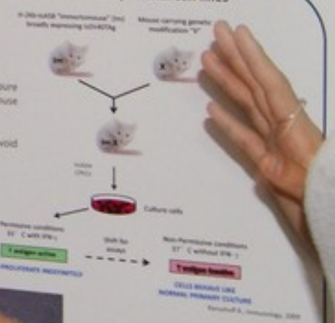
Light microscopy of a 1 week culture: a confluent cell monolayer

Schematic representation of junctional complexes in CPECs.

Immunofluorescence: continuous tight junctions



Establishment of choroid plexus epithelial cell lines



Primary CPEC culture: highly pure BUT: output of 12-15 mouse brains is $5x10^5$ cells only!

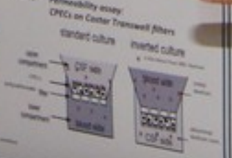
→ CP epithelial cell line to avoid repeated killing of mice

Light microscopy of immorto CPECs grown under permissive conditions: immortalized behaviour and a fibroblast like morphology. A differentiation has not sucessfully been

Characterization of the CPEC barriers

Physiological migration of immune cells across the CP

Permeability assay: CPECs on Costar Transwell filters



standard culture

inverted culture

BCSFB:

- Which cells can pass through it?
- Which trafficking molecules on the CPECs and on the immune cells are involved?

Single cell resolution, quantitative measurements in 3-dimensional datasets of entire lymphoid tissue using laser sheet microscopy

INTRODUCTION

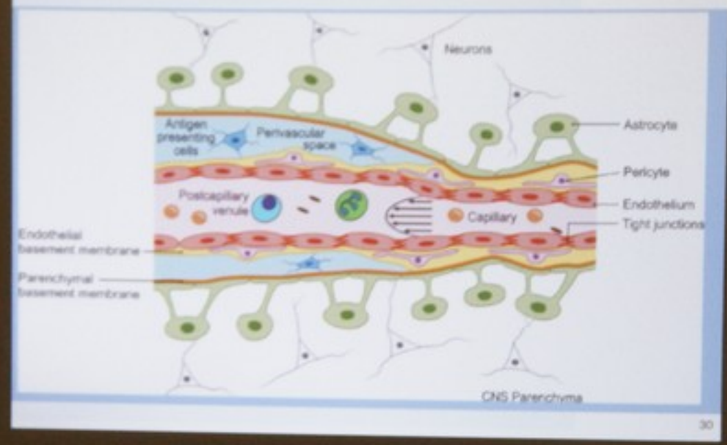
EXPERIMENTAL SET-UP

RESULTS


The Blood Brain Barrier:
Checkpoint Charlie for Immune Cell Entry
into the CNS
Britta Engelhardt
Theodor Kocher Institute
University of Bern
Switzerland

The blood-brain barrier:

Checkpoint Charlie for immune cell entry into the CNS



30

Granule Serine Proteases and Serpins:
Fine tuning cell survival and inflammation

Charaf Benarafa, DVM PhD
Theodor Kocher Institute

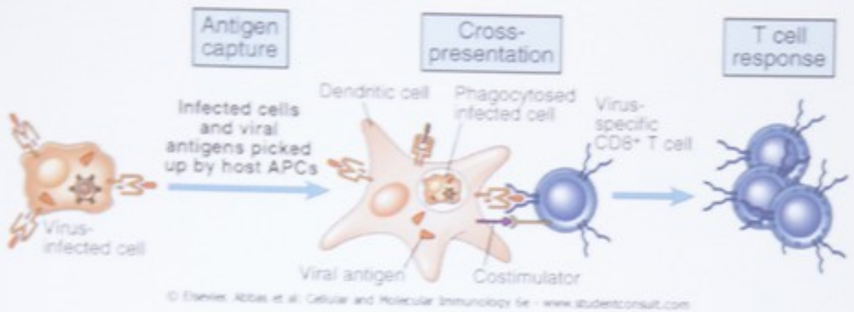
th International BIC Summer School,
Bönigen, 12-14.08.2012

Overexpression of BCL-2 in the granulocyte lineage induces an AML like, neutropenic phenotype

Summer School 2012

MATHIAS BAUMANN
THEODOR KOCHER INSTITUTE
BENARAFA GROUP

Adaptive immunity relies on intercellular communication



DOCK8 in T cell migration
&
effector cell differentiation

Summer School 2012

14.08.2012
Markus Pieczyk
Theodor-Kocher-Institute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