

Poster sessions

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1 EVA NAUMANN

Uncovering tumor-intrinsic immune evasion in neuroblastoma using 3D spheroids

Florian Köhldorfer, Benjamin Schattling, Ingo Müller

Neuroblastoma (NB), the most common extracranial solid tumor in children, remains a major clinical challenge in pediatric oncology. Despite intensive multimodal therapy, patients with high-risk disease frequently relapse and long-term outcomes remain poor. Immunotherapy with monoclonal antibodies targeting the ganglioside GD2 has improved survival; however, severe side effects and limited efficacy in relapsed disease highlight the need for more effective therapeutic strategies.

A major barrier to successful immunotherapy in solid tumors is the complex tumor microenvironment, which can limit effector-cell infiltration, promote immune inhibition, and facilitate antigen- or therapy-associated resistance. Conventional two-dimensional (2D) cell culture systems only partially capture these features.

To better understand and overcome these resistance mechanisms, robust and physiologically relevant disease models are required. In this study, we establish three-dimensional (3D) neuroblastoma spheroid models as an intermediate platform between conventional two-dimensional (2D) cell culture and in vivo models to investigate tumor-intrinsic and spatially organized mechanisms of immune resistance.

Spheroid culture conditions were optimized to generate reproducible neuroblastoma spheroids resembling key features of small avascular tumors. Model validation by immunofluorescence staining demonstrated spatial differences in proliferation, apoptosis, and necrosis. Confocal microscopy further revealed pronounced extracellular matrix (ECM) deposition surrounding the spheroids, suggesting that the model captures structural barriers relevant to antibody-based immunotherapy.

Functionally, 3D-cultured neuroblastoma cells exhibited increased resistance to complement-dependent cytotoxicity (CDC), antibody-dependent cell-mediated cytotoxicity (ADCC) and CAR-NK cell mediated cytotoxicity compared to conventional 2D cultures. These findings suggest that this model captures key tumor-intrinsic mechanisms of immune evasion.

Ongoing spatial transcriptomic analyses will compare 2D and 3D cultures across neuroblastoma cell lines and treatment conditions to identify molecular pathways associated with immune escape and potential therapeutic vulnerabilities.

Together, these data establish neuroblastoma spheroids as a tractable 3D model to study spatial, extracellular-matrix-associated, and molecular determinants of resistance to immunotherapy.

2 CELINE PÖHLKING

Novel naturally occurring antibodies against neuroblastoma

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Neuroblastoma is the most common extracranial solid tumor in children and is characterized by extensive genomic alterations that drive tumor heterogeneity and progression. Patients diagnosed after infancy frequently develop metastatic disease and face poor clinical outcomes. Gangliosides, sialic acid-containing glycosphingolipids expressed on neuroblastoma cells, are attractive immunotherapeutic targets. While anti-GD2 monoclonal antibody therapy has improved survival, approximately one-third of patients do not respond, and treatment is often associated with severe neuropathic pain due to GD2 expression on peripheral nerves.

Screening of serum from healthy donors previously identified naturally occurring antibodies with potent cytotoxic activity against neuroblastoma cells. Among these candidates, antibodies directed against specific gangliosides were detected. To identify therapeutically relevant antibodies, we developed a workflow for the purification and sequencing of ganglioside-specific serum antibodies. Antibody activity is monitored throughout the purification process using neuroblastoma cell-based cytotoxicity assays and a newly established ganglioside-specific ELISA. Affinity purified antibodies are subsequently characterized by mass spectrometry, and selected sequences are recombinantly expressed for in vitro validation.

Naturally occurring ganglioside-targeting antibodies represent a promising alternative to current GD2-directed therapies. As these antibodies are present in healthy individuals without apparent adverse effects, they may provide improved tumor specificity while reducing off-target toxicity. This approach may enable the development of safer and more effective antibody-based immunotherapies for neuroblastoma.

3 ANDREI LAZAR

Age-dependent single-cell immunome and roles of $\gamma\delta$ T cells in pigs

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Species with high frequencies of $\gamma\delta$ T cells in the blood, such as pigs, exhibit an expansion of γ and δ chain genes. These species also diversify co-receptors, suggesting important functions of $\gamma\delta$ T cells in host immunity. To investigate the roles of $\gamma\delta$ T cells, including their influence on the immune cell landscape, we profiled $\gamma\delta$ T cell knockout (KO), heterozygous (HET) and age-matched wild-type (WT) piglets as they progressed from the juvenile to the subadult age. We observed similar frequencies of $\gamma\delta$ T cells in WT and HET piglets. The frequencies of CD4+CD8+ $\alpha\beta$ T cells, including a subset expressing CD11a, were enriched in WT compared to KO or HET piglets. In line with our previous observations of higher vaccine induced antibody titers in WT pigs, we detected more abundant B lymphocytes in younger WT piglets. In separate cohorts, we profiled adult animals. We observed lower frequencies of $\gamma\delta$ T cells in HET adult pigs in comparison to WT counterparts as well as higher frequencies of total CD4+ $\alpha\beta$ T cells in adult KO and HET pigs than in WT animals. Myeloid cell populations were comparable for all genotypes and ages. Preliminary results suggest a stronger lymphocyte proliferation response to mitogens in KO pigs. We are currently analyzing scRNA seq datasets from transgenic and WT pigs which will offer comprehensive insights into immune cell subsets, and into the impact of $\gamma\delta$ T cell deficiency on functional states of pig leukocytes. These findings will improve our understanding of $\gamma\delta$ T cells in mammals and facilitate modulation of the pig immune system to enhance health and vaccination outcomes

4 LOUISA E. NEUMANN

Inhibition of autophagy promotes hepatitis E virus replication

Daniel Todt, Eike Steinmann, Toni L. Meister

Autophagy is a fundamental cellular process that maintains homeostasis by degrading and recycling components such as damaged organelles, misfolded proteins and other macromolecules and cellular components. Additionally, it also contributes to the host immune system by pathogen clearance through direct degradation of intracellular microbes and activation of downstream immune signaling. However, several viruses use the autophagic machinery to promote their own life cycle and benefit their virion production. Many pathogens have evolved individual strategies to exploit or circumvent this pathway: For instance, flaviviruses, coronaviruses and human immunodeficiency virus activate and manipulate autophagic membranes to build replication complexes or mediate non-lytic release, turning the degradative pathway into infrastructure for viral propagation. Other Viruses, such as human cytomegalovirus, herpes simplex virus-1 and Epstein-Barr virus counteract autophagy and interfere with autophagy receptors such as p62/SQSTM1 to escape selective autophagic degradation. Understanding the molecular basis of these interactions is crucial for developing therapeutic strategies that can modulate autophagy to enhance host defence mechanisms against various viral infections.

5 ALIN MISHEL HERNANDEZ BUSTOS

HIV-1 infection of cerebral organoids: establishment of a human in vitro model.

K. Schiering, U. Lange, A. Hölzemer.

The brain reservoir represents a potential obstacle to HIV cure research, given the risk of neuroinflammatory damage upon virus reactivation. Due to the inaccessibility of the human brain, mainly non-human models like humanized mice or primates have been studied in Neuro-HIV. However, 3D brain organoid models, derived from human iPSCs, contain multiple neural and glial cell types allowing the development of a brain-like architecture and offering a human platform for studying Neuro-HIV infection. In order to test different therapeutic options targeting the brain reservoir, we characterized a microglia-containing human cerebral organoid model for HIV infection.

6 DIMITRIOS NIKOLAOS KAPIRIS

Interactions between lung microenvironment and immune responses in the sex-specific manifestation of asthma

Dimitrios Nikolaos Kapiris , Eleftherios Papazoglou , Klearchos Stampolitis, Handai Xia, Petra C. Arck, Samuel Huber, Anastasios Giannou and Dimitra E. Zazara

Asthma is one of the most widespread chronic inflammatory diseases and its prevalence is constantly rising. cClinical presentation of asthma is characterized by profound age-dependent sex-specific differences, with males suffering more often in childhood, while in adolescence and adulthood, asthma affects mostly females. Studies suggest that sex hormones, particularly androgens, contribute to these differences in asthma and may modulate disease severity and immune responses. populations. However, little is known about the potential sex bias characterizing tissue-resident immunity and the contribution of sex hormones and age progression to this. We aim to understand how sex differences in the lung local microenvironment contribute to the age-dependent sexual dimorphism of asthma and pinpoint the role of sex hormones in this context.

7 KLEARCHOS STAMPOLITIS

Gut microbiome signatures associated with liver metastasis in colorectal cancer

Klearchos Stampolitis, Natasha Irene Schweitzer, Eleftherios Papazoglou, Jöran Lücke, Yunhe Tang, Siwen Zhang, Dimitris-Nikolaos Kapiris, Morsal Sabihi, Dimitra E. Zazara, Penelope Pelczar, Samuel Huber, Anastasios Giannou

Colorectal cancer liver metastasis (CRLM) remains a major cause of cancer-related mortality. Increasing evidence suggests that the gut microbiome can influence distant tumour progression by modulating systemic and tissue-specific immune responses. However, the mechanisms by which dysbiotic microbial communities shape the hepatic microenvironment and promote metastatic growth remain incompletely understood.

We investigated the impact of distinct gut microbiota on liver metastasis using microbiota-colonized mouse models followed by intrasplenic injection of colorectal cancer cells. Conventional microbiota were compared with multiple dysbiotic communities. Liver immune composition was assessed by multiparameter flow cytometry before and after tumour challenge. In parallel, 16S rRNA sequencing was used to identify bacterial signatures associated with metastatic phenotypes in mice and human colorectal cancer samples.

Mice colonized with dysbiotic microbiota consistently developed an increased liver metastatic burden compared with controls. Importantly, immune profiling revealed microbiota-dependent alterations in the hepatic immune compartment.

Cross-species microbiome analysis identified bacterial families enriched across metastasis-associated mouse microbiota, while human colorectal tumour samples showed enrichment of specific taxa. Functional metagenomic profiles were predicted to identify microbiome-associated metabolic pathways potentially linked to liver metastasis.

Our findings support a model in which gut dysbiosis promotes CRLM by preconditioning the hepatic immune microenvironment. Ongoing studies aim to define the responsible bacterial taxa and microbiota-driven immune pathways and to evaluate their therapeutic potential.

8 LISBETH HASLER

Developmental origin and plasticity of sex-specific immunity against pathogens

I. belios, c. urbschat

Foetal immune development is modulated by challenges of the modern environment, such as high maternal stress perception. In turn, prenatal stress increases the risk of infections later in life of the offspring. Surprisingly, the offspring's sex has been overlooked in most of these studies, despite the well-known sex disparities in infection risks. We aim to close this gap in knowledge. We hypothesize that prenatal stress exposure causes variation of the sex-specific disease tolerance to pathogens in offspring and differentially affects immunity to pathogens throughout postnatal life of male and female offspring. We also hypothesize that such variations of sex-specific immunity to pathogens segue into evolutionary trade-offs.

9 FELIX HILDEBRAND

Angiotensin II-induced hypertension alters cytokine levels in the brain

Felix Hildebrand 1, 2, Jorge Enrique Duque Escobar 3, 4, Olga Schweigert 3, 4, Tina Fischer 1, 2, Karolin Gustmann 1, Tanja Zeller 3, 4, Mathias Gelderblom 1, Tim Magnus 1, Karoline Degenhardt 1

The cardiovascular risk factor hypertension represents a key predisposition for stroke and is a major contributor to chronic inflammation. Microglia, the resident immune cells of the central nervous system, exhibit pronounced phenotypic plasticity and can adapt their functional state in response to inflammatory cues, thereby influencing neurological disease outcomes. We hypothesized that hypertension-induced systemic inflammation modulates the microglial phenotype, affecting microglial responses towards stroke pathology. To test this hypothesis, we employed peripheral infusion of Angiotensin II (Ang II) in a fast pressor model (1000 ng/kg/min for 14 days) and a slow pressor model (200 ng/kg/min for 14 days and 490 ng/kg/min for 14 days) to assess the impact of hypertension on brain cytokine profiles and microglial morphology. Our analyses revealed that hypertension increases the concentrations of pro-inflammatory cytokines and neutrophil-attracting chemokines in the brain after Ang II infusion, whereas its effects on microglial morphology remain inconclusive. Collectively, these findings highlight a substantial influence of systemic hypertension on the inflammatory brain environment, while a direct impact on microglial phenotype requires further investigation. Future multiomic analyses of the microglial transcriptome and epigenome will help to determine whether hypertension induces an altered genetic program driving microglial adaptations which affect their reactivity towards stroke pathology.

10 BARSA DAL

Selective enhancement of the interferon response in the trisomy 21 thymus

Barsa Dhal, Annika Boxnick, Laura Glau, Lena Rüscher, Babett Steglich, Manuela Kolster, Romy Hackbusch, Ida Hüners, Martin Munz, Sebastian Schloer, Nicola Gagliani, Christian Krebs, Jörg Sachweh, Michael Hübner, Anna Gieras, Eva Tolosa

Trisomy 21 (T21), the genetic cause of Down syndrome, is associated with immune dysregulation. Infants with T21 have a small, structurally abnormal thymus, suggesting impaired T-cell development. T21 is also considered a chronic interferonopathy, attributed to increased dosage of chromosome 21-encoded type I interferon (IFN) receptor genes and elevated IFN signaling in peripheral immune cells. However, the contribution of type I IFNs to altered thymocyte development in T21 remains unclear. Using CITE-seq, we found an elevated type I IFN transcriptional signature in thymocytes from individuals with T21, most pronounced during early T-cell development and in mature thymocytes. Validation by qPCR showed increased transcript levels of the chromosome 21-encoded genes IFNAR1, IFNAR2, MX1, and MX2, whereas IFN-related genes located on other chromosomes showed only modest increases or no change. These findings suggest a selective, rather than broadly amplified, IFN-associated transcriptional program in the T21 thymus. We used SCENIC analysis of the RNA transcriptome to infer the activity of the regulons downstream of IFNAR signalling, and found that STAT1 and STAT2 regulons are more active in T21 thymocytes. To assess IFN responsiveness, we stimulated thymocytes with IFN α 2 and measured IFN-stimulated gene (ISG) expression. Following stimulation, MX1 and MX2 expression was higher in T21 than in disomy 21 (D21) thymocytes, whereas expression of ISGs encoded on other chromosomes was comparable between groups. Notably, IFN α and IFNB1 transcript levels were markedly elevated in T21 thymic tissue, consistent with higher local IFN production contributing to the enhanced basal IFN signature rather than generalized thymocyte hyperresponsiveness. Finally, we found that IFN α 2 negatively affects IL-7-induced proliferation of thymocytes. Together, these findings reveal elevated expression of chromosome 21-encoded IFN receptor genes and a heightened basal IFN-associated transcriptional program without broad enhancement of ISG expression or responsiveness. Increased local IFN production, together with chromosome 21 gene dosage effects, may contribute to impaired thymopoiesis and immune dysfunction in individuals with T21.

11 MIRIAM TOMCZAK

Bile acid-mediated ileal barrier function deficits in primary sclerosing cholangitis

Miriam Tomczak, Katherine Coldwell, Kyla Dooley, Amelia Heslington, Claire Pearson, Elizete Araujo, Megan Perry, Kaye Eve-Rowe, Shana-Lee Bownes, Yukari Kimura, Nicholas Provine, Lisa Gartner, Amy Cross, Joanna Hester, Iolanda Vendrell, Anna Hoyle, Roman Fischer, Sandi Yen, Charlotte Rich-Griffin, Ida Parisi, Oyindamola Ajisegiri, Sumaiya Hoque, TGLU investigators, Human Cell Atlas (HCA) investigators, Fadi Issa, Samuel Huber, Fiona Powrie, Matthias Friedrich, Holm Uhlig, Calliope Dendrou, Emma L Culver, Paul Klenerman and Nicholas Iliott

Anatomical resolution of intestinal barrier deficits in PSC and related chronic liver diseases is lacking. This study reveals a potential new source of barrier integrity deficit in the terminal ileum.

We show that the phase II detoxification gene, Glutathione-S-transferase alpha 1 (GSTA1) marks one enterocyte state that is enriched at the base of villi in the terminal ileum and is co-expressed with multiple other detoxification enzymes. Genes within this co-expression module are downregulated in ileal samples from patients with PSC-UC. We confirm that *Gsta1* mRNA is decreased in the ileum in murine cholestatic liver disease and altering microbiome capacity for bile acid deconjugation can regulate *Gsta1* expression.

These findings represent potential new targets for microbiome-based treatments that alter bile acid modifications to improve barrier function.

12 FREYA SIBBERSTEN

Phenotypic and clonal profiling of $\gamma\delta$ T cells in human kidney and liver

Freya Sibbertsen¹, Datev Nahapetyan¹, Robin Kathri¹, Darius Schraub¹, Cedric Ly¹, Zheng Song¹, Zeba Sultana¹, Meike Petersen¹, Stefan Bonn¹, Kevin Paul¹, Camilla Engblom², Ulf Panzer¹, Christian Krebs¹ and Immo Prinz

$\gamma\delta$ T cells are unconventional lymphocytes capable of responding rapidly to infection, cellular stress, and tissue damage. However, their phenotypic adaptation, clonal distribution, and spatial organization within human solid organs remain poorly understood. We analyzed $\gamma\delta$ T cells in kidney biopsies and pediatric liver explants and compared them with peripheral blood using flow cytometry, single-cell transcriptomics, V(D)J sequencing, and spatial transcriptomics.

We identified $\gamma\delta$ T cells in kidney and liver. Tissue $\gamma\delta$ T cells displayed a more mature, activated, and tissue-resident phenotype than circulating $\gamma\delta$ T cells. Using the CDR3 sequences as clonal barcodes, individual $\gamma\delta$ T-cell clones could be tracked across blood and tissue, even from small biopsy samples.

Our findings highlight the distinct phenotypic and clonal characteristics of $\gamma\delta$ T cells in human solid organs. Integrating single-cell and spatial analyses provides an interesting way to understand how local tissue environments shape $\gamma\delta$ T cell differentiation and function.

13 VICTORIA TENNERT

Maternal cytomegalovirus infection – The impact of maternal immune activation on placental integrity and foetal development

Emily Kerth, Luís Fonseca Brito, Eléonore Ostermann, Wolfram Brune, Felix Stahl

Human cytomegalovirus (HCMV) is a widespread pathogen, with a worldwide seroprevalence of 50-100%. HCMV can cross the placenta and lead to congenital infection (cCMV), the major infectious cause of neurological impairment in newborns. Even without vertical transmission, viral infections can trigger maternal immune activation (MIA), which has been linked to adverse fetal outcomes such as disrupted hematopoiesis, immune dysfunction, miscarriage, and stillbirth. The molecular mechanisms underlying these effects remain to be understood.

This project investigates the impact of CMV-induced MIA on maternal and offspring health in mice. The murine CMV (MCMV) cannot cross the placenta, so any observed effects in MCMV-exposed fetuses can be attributed to immune activation rather than direct infection of the offspring. To differentiate CMV-specific effects from other virus-induced immune activation, we will also assess maternal infection with Modified Vaccinia virus Ankara (MVA) and Influenza A virus (IAV). We will use a multiparametric profiling approach including flow cytometry, proteomics, and histopathological analysis to assess the impact of maternal virus infection on the immune system, placenta barrier function, and offspring's health. This integrated approach will clarify how virus-induced inflammation affects the maternal-foetal interface and causes disadvantageous pregnancy outcomes. Identifying MIA-associated molecular pathways may reveal therapeutic targets to protect placental and offspring health and could uncover biomarkers for predicting pregnancy outcomes during viral infections.

14 IRIS CORREIA RAMOS, TWISHA KEJRIWAL

Balancing tissue-resident immunity in the uterus: interplay between TRM cells and regulatory T cells during pregnancy

Íris Correia Ramos, Twisha Kejriwal, Dennis Yüzen, Nicola Gagliani, Petra Clara Arck, Hans-Willi Mittrücker, Kristin Thiele

During pregnancy, a unique and tightly regulated maternal immune adaption is required to ensure tolerance toward the semi-allogeneic fetus. Our aim is to investigate the effect of maternal immune activation (MIA) on T cells in the uterus, and its subsequent impact on fetal development and pregnancy outcome. We have established a mouse model, with pre-conceptual priming, which enables tracking activation status and cytokine production of uterine regulatory T cells (Tregs) and tissue resident T cells (TRM cells), including paternal antigen-specific T cells, during a healthy pregnancy, and later, upon MIA.

15 DATEV NAHAPETYAN

Spatial Transcriptionomics Analysis of postnatal Human Thymus

Datev Nahapetyan †, Cedric Ly †, Darius P. Schaub, Enrico Kittman , Stefan Bonn , Ulf Panzer, Christian Krebs, Eva Tolosa, Immo Prinz

During T-cell development, somatic recombination of V(D)J gene segments generates a vast diversity of T-cell receptor variable (TRV) genes, including alpha (TRAV), beta (TRBV), delta (TRDV) and gamma (TRGV) chain sequences. Resolving this recombination process spatially, within intact tissue architecture, offers a direct view of the cellular dynamics of thymopoiesis and of its microenvironmental context that cannot be recovered from dissociated single-cell data. To address this, 132 TRV-targeting in situ hybridization probes previously validated in kidney tissue were quality-tested on formalin-fixed paraffin-embedded (FFPE) and fresh-frozen (FF) postnatal human thymus profiled with the 10x Genomics Xenium platform. Because the extreme cellular density of the thymus makes conventional cell segmentation unreliable, probe performance was evaluated with a transcript-centric, segmentation-free framework built on DBSCAN clustering, combined with a modified version of TissueTag2 for cortico-medullary spatial annotation. This pipeline retained 38 high-confidence probes capable of detecting TRV gene expression in situ. As proof of concept, we show that these probes track the sequential $\beta \rightarrow \alpha$ rearrangement programme across the cortico-medullary axis and can be used to characterise the surrounding microenvironment. These results establish a validated spatial toolset for studying T-cell receptor diversity and thymic biology at tissue resolution.

16 PETER BRADKE

ADAM10-deficiency in iNK T cells results in an aggravated α -GalCer-induced liver inflammation in mice

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ADAM10 (A Disintegrin And Metalloproteinase 10) is a membrane-bound metalloproteinase constitutively expressed on T cells. Substrates of ADAM10 on T cells include NOTCH family members, FasL and IL-2R α . Although these substrates indicate a role of ADAM10 in T cell function, the relevance of ADAM10 for T cell responses is still largely unclear. To study the role of ADAM10 in vivo , Adam10 x CD4Cre mice with a T cell restricted deletion of Adam10 were generated. Focusing on iNK T cells, a blockade during thymic maturation was observed in both CD4 and CD4 iNK T cells, and a general reduction of CD4 iNK T cells was noted. These findings were recapitulated in peripheral iNK T cell populations. ADAM10-deficient iNK T cells in liver and spleen displayed a more activated phenotype at steady state. Upon treatment with the iNK T cell antigen α -galactosylceramide (α -GalCer), Adam10 x CD4Cre mice showed a significantly lower cytokine response. However, the α -GalCer treatment still led to an aggravated liver inflammation in Adam10 x CD4Cre mice, marked by significantly higher AST and ALT serum levels and enlarged areas of hepatocyte damage. Analysis of ADAM10-deficient iNK T cells from α -GalCer-treated mice revealed a higher surface expression of the ADAM10 target FasL, which may be responsible for the substantial killing of Fas-expressing hepatocytes. Conclusively, our results identify a crucial role of ADAM10 for the maturation and function of iNK T cells.