

# **Münster Drosophila Mini-Symposium**

## **Reporte der Beiträge**

Beitrag ID: 3

Typ: **talk**

## Glial-dependent clustering of voltage-gated ion channels in *Drosophila* precedes myelin formation

*Dienstag, 7. März 2023 17:15 (12 Minuten)*

Neuronal information conductance depends on transmission of action potentials. The conductance of action potentials is based on three physical parameters: The axial resistance of the axon, the axonal insulation by glial membranes, and the positioning of voltage-gated ion channels. In vertebrates, myelin and channel clustering allow fast saltatory conductance. Here we show that in *Drosophila melanogaster* voltage-gated sodium and potassium channels, Para and Shal, co-localize and cluster in an area of motor axons resembling the axon initial segment. Para but not Shal localization depends on peripheral glia. In larvae, relatively low levels of Para channels are needed to allow proper signal transduction and nerves are simply wrapped by glial cells. In adults, the concentration of Para at the axon initial segment increases. Concomitantly, these axon domains are covered by a mesh of glial processes forming a lacunar structure that serves as an ion reservoir. Directly flanking the voltage-gated ion channel rich axon segment, the lacunar structures collapse forming a myelin-like insulation. Thus, *Drosophila* development may reflect the evolution of myelin which forms in response to increased levels of clustered voltage-gated ion channels.

**Hauptautoren:** REY, Simone (Neurobiologie); OHM, Henrike (Neurobiologie); Prof. KLÄMBT, Christian (Neurobiologie)

**Vortragende(r):** REY, Simone (Neurobiologie)

Beitrag ID: 5

Typ: **talk**

## **Bivalent heparan sulfate interactions determine Hedgehog morphogen gradient robustness and range: A general mechanism for extracellular protein distribution?**

*Dienstag, 7. März 2023 13:45 (12 Minuten)*

Communication between cells is essential for unimpaired metazoan development and physiology. Hedgehogs (Hh) are one example of a highly conserved family of secreted morphogens that regulate vertebrate and invertebrate development directly and in concentration-dependent manner. It is known that Hhs need to associate with heparan sulfate (HS) chains on the plasma membrane of producing cells as one essential prerequisite for their subsequent release and spread through HS-rich tissues. This, in turn, determines Hh gradient formation, gradient range and gradient robustness. The mechanistic basis of HS-regulated Hh gradient formation and function, however, is only poorly understood. Here we use Quartz crystal microbalance with dissipation monitoring (QCM-D) and advanced *Drosophila melanogaster* genetics to show that HS-mediated Hh spread and gradient formation require directed charge-dependent Hh diffusion on HS and the ability of Hh to switch between HS chains by using two highly conserved HS binding sites. Interfering with one of the two HS binding sites of Hh strongly disturbs Hh gradient robustness and range and leads to ectopic target gene expression, tissue overgrowth and mirror-image duplications of tissues. We suggest that ectopic signaling results from Hh loss from HS into the extracellular space, possibly caused by aborted switching between HS chains during Hh transport. Hh “leakage” would then induce ectopic Hh target gene expression. Finally, we show that HS-restricted Hh diffusion may provide a blueprint for the extracellular transport of a variety of proteins, including morphogens, growth factors of the fibroblast growth factor family, chemokines, or SARS-CoV-2 spike proteins that also bind HS.

**Hauptautoren:** Prof. GROBE, Kay; Herr FROESE, Jurij; Dr. MANIKOWSKI, Dominique; Dr. STEFFES, Georg; Dr. DANIELE DI IORIO; Herr GUDE, Fabian

**Vortragende(r):** Herr GUDE, Fabian

Beitrag ID: 6

Typ: poster

## The opposing chloride cotransporters KCC and NKCC control locomotor activity in constant light and during long days

Dienstag, 7. März 2023 20:00 (12 Minuten)

Cation chloride cotransporters (CCCs) are evolutionary conserved proteins mediating the electroneutral transport of Cl<sup>-</sup>, K<sup>+</sup> and/or Na<sup>+</sup>. While KCCs export chloride out of the cell, the opposing N(K)CCs function as chloride importers. Their activity is reciprocally regulated by phosphorylation through chloride-sensitive Wnk and SPAK/OSR1 (*D.m.*: Fray) kinases, resulting in tight regulation of the intracellular chloride level [Cl<sup>-</sup>]<sub>i</sub>. Normally, [Cl<sup>-</sup>]<sub>i</sub> is low, whereby binding of GABA to the ionotropic GABA-A receptor results in neuronal inhibition through chloride influx. However, when [Cl<sup>-</sup>]<sub>i</sub> is high, GABA can also exert an excitatory response. In the mammalian SCN expression and activity of NKCC and KCC underlie daily and regional variations. Resulting differences in GABA polarity have been shown to contribute to light-dependent synchronization of the circadian clock, e.g. phase delaying in response to a light pulse and adaptation to seasonal changes in day length. Previous studies indicate similar mechanisms may operate in the fly clock system, where NKCC is known to influence light-input and GABA responses in clock neurons (Buhl et al. 2016 PNAS). Here we provide further evidence for the role of KCC and Wnk/Fray in regulating GABA responses and behavioral light responses (Eick et al. 2022 Current Biology). While wild type flies become arrhythmic under constant light (LL), up- or downregulation of KCC, Wnk and Fray led to robust locomotor rhythms in LL, indicating their requirement for normal light-input to the clock. Next, we measured the GABA-induced currents in l-LNv clock neurons to calculate the GABA reversal potential EGABA. As expected, KCC overexpression lowered EGABA, while *kcc* knockout resulted in a more positive EGABA, changing GABA into an excitatory neurotransmitter. Finally, we recorded the locomotor activity under long days. All flies were able to adapt to a longer photoperiod, but while *NKCC* knockout flies exhibited an abnormal increase in activity during the early morning, activity was notably reduced in *kcc* knockout flies at that time. All in all, our results suggest that regulation of [Cl<sup>-</sup>]<sub>i</sub> in clock neurons via CCCs is a conserved mechanism that is crucial for normal clock function.

**Hauptautoren:** EICK, Anna Katharina (Institute of Neuro- and Behavioral Biology, WWU); OGUETA, Maite (Institute of Neuro- and Behavioral Biology, WWU); BUHL, Edgar (School of Physiology, Pharmacology and Neuroscience, University of Bristol); Prof. HODGE, James (School of Physiology, Pharmacology and Neuroscience, University of Bristol); Prof. STANEWSKY, Ralf (Institute of Neuro- and Behavioral Biology, WWU)

**Vortragende(r):** EICK, Anna Katharina (Institute of Neuro- and Behavioral Biology, WWU)

Beitrag ID: 7

Typ: **talk**

## Zeitgeber or non-Zeitgeber that is the circadian question

*Dienstag, 7. März 2023 17:30 (12 Minuten)*

The circadian clock allows organisms to stay in sync with their ecological niche. Virtually, all organisms from bacteria to humans, have an endogenous circadian clock that ticks with a period of about 24h. In order to stay synchronised, the circadian clock uses rhythmic environmental parameters (also called Zeitgeber) for its resetting (entrainment), the main ones being light and temperature. However, both light and temperature varies in an unpredictable manner and depending on the time of day, organisms can respond differently to these changes. How does the circadian system distinguish between Zeitgeber and non-Zeitgeber input?

To tackle this important question and yet still unresolved today, I am entraining the flies using temperature cycles (25°C-16°C) as Zeitgeber and study how the light input modulates the rhythmic and synchronised locomotor activity pattern. Both the canonical visual pathway and the circadian blue light photoreceptor CRYPTOCHROME can entrain to light-dark cycle the circadian clock in the brain and synchronised the locomotor activity. However, we do not know whether and how the light information they are providing can be taken as a non-Zeitgeber input.

**Hauptautor:** Dr. LAMAZE, Angélique Elénore Guy

**Vortragende(r):** Dr. LAMAZE, Angélique Elénore Guy

Beitrag ID: 8

Typ: talk

## Drosophila as a model system for atypical teratoid/rhabdoid tumors

Dienstag, 7. März 2023 14:00 (12 Minuten)

Atypical teratoid/rhabdoid tumors (ATRTs) are highly malignant brain tumors, mainly affecting infants and children. Mutations causing loss of SMARCB1 function, a core component of SWI/SNF chromatin remodeling complex are a hallmark genetic feature. Even though other recurrent genetic alterations are absent, ATRTs are highly heterogeneous with regard to epigenetic features, gene expression profiles and clinical features. Based on DNA methylation profiles, ATRTs segregate into three molecular groups, i.e. ATRT-TYR, ATRT-MYC and ATRT-SHH. ATRT-SHH represents the largest molecular group and is characterized by active sonic hedgehog and notch pathways. In contrast to other cancers, however, mutations in sonic hedgehog and notch related genes are not encountered and little is known about mechanisms involved in dysregulation of these pathways relevant for tumor formation, maintenance and progression upon SMARCB1- deficiency.

In order to explore the role of hedgehog (hh) and notch pathway dysregulation upon SMARCB1-deficiency, we used *Drosophila melanogaster* as a model. We applied UAS/GAL4 system to knock down *Snr1*, the fly homolog of SMARCB1, in the wing disc of *Drosophila* larvae. In contrast to ubiquitous (*Tubulin*- or *Actin*- GAL4), wing disc specific (*ms1096* and *ap*- GAL4) or *hh* repressed regions (*ptc* or *dpp*-GAL4), tumor-like structures developed when *Snr1* was down regulated in the posterior, *hh* expressing region (*en*- or *hh*-GAL4). Presence of such features was accompanied by abnormalities in hh and notch pathway activation. Furthermore, in affected regions not only proliferation but also cell cycle was disrupted, underlining the role of *Snr1* in growth control. Remarkably, a high diversity of phenotypes was encountered, suggesting clonal aspects and involvement of other genes. Further studies are required to identify these genes in modifier screens i.e. testing fly orthologs of genes up-regulated in ATRT and active in the wing imaginal discs.

**Hauptautor:** MISKIEWICZ, Katarzyna

**Co-Autor:** Prof. HASSELBLATT, Martin

**Vortragende(r):** MISKIEWICZ, Katarzyna

Beitrag ID: 9

Typ: **poster**

## Spectraplaklin Couples Microtubule Orientation to Actin During Dendritic Pruning

Dienstag, 7. März 2023 19:45 (12 Minuten)

Neurite pruning, the elimination of specific axonal or dendritic branches, is an essential mechanism to refine developing neural circuitry. Following local microtubule and actin disassembly, *Drosophila* sensory c4da neurons prune their dendrites during metamorphosis. We previously found that the uniform plus end-in orientation of dendritic microtubules is required for efficient pruning by enabling their coordinated disassembly. How dendritic microtubule organization is established is only incompletely understood. Here, we show that the spectraplaklin short stop (Shot), an actin-microtubule crosslinker, is required for c4da neuron dendritic pruning. We find that Shot genetically interacts with known factors governing dendritic microtubule organization, and loss of Shot itself misorients dendritic microtubules. Forced actin depolymerization also causes dendritic microtubule orientation defects, and the actin binding ability of Shot impinges on microtubule orientation. Finally, we show that inhibition of actin depolymerization during pruning also inhibits microtubule disassembly, indicating coordination of local cytoskeleton disassembly. Our data suggest that via Shot-mediated coupling, actin is necessary for establishing plus end-in microtubule orientation in dendrites, facilitating pruning.

**Hauptautor:** DAVIES, Matthew (University of Münster)

**Co-Autoren:** Dr. WOLTERHOFF, Neele (Freie Universität Berlin); Dr. RUMPF, Sebastian (University of Münster)

**Vortragende(r):** DAVIES, Matthew (University of Münster)

Beitrag ID: 10

Typ: poster

## Temporal niche choice in *Drosophila melanogaster*

Dienstag, 7. März 2023 19:30 (12 Minuten)

In a world characterized by regular fluctuations, biological systems have developed mechanisms to anticipate and respond to environmental changes to increase their fitness and survival. Circadian clocks consist of highly preserved molecular feedback loops allowing organisms to adapt their behavior to the 24 hours environmental light and temperature changes. Circadian clocks enable biological

systems to restrict their activity to specific periods of the day, which is defined as temporal niche. Correct temporal niche choice is important for the fitness and survival of an organism, and it is regulated by an intricate interplay between the animal's circadian clock and environmental fluctuations.

As temporal organization is genetically determined, mutations in circadian clock genes can allow organisms to explore and to occupy different temporal niches, increasing the adaptation of a population to different environmental conditions. However, the molecular and cellular mechanisms that

drive niche choice remain to be fully understood. Under non-stressful conditions, individuals show low inter-specific phenotypic variability, despite being genetically different. However, they may accumulate genetic mutations that are not phenotypically visible, called cryptic genetic variations. When a sudden environmental stressor occurs, cryptic genetic variations introduce new phenotypes

that are then bottlenecked by natural selection to favor fitness and survival of the population. Heat shock protein 90 (HSP90) has been identified as a possible candidate to unveil the genetic potentials of biological systems. Previous studies (Hung et al., 2009) indicate that loss of HSP90 leads to increased behavioral variation in *Drosophila*, including multiple transitions from rhythmic to arrhythmic behavior. Here, we investigate

whether individuals can actively explore and choose temporal niches that support their own fitness,

and the possible role of HSP90 in the molecular pathways leading to variable intraspecific temporal

niche choices.

**Hauptautoren:** COCULLA, Angelica (Institute of Neuro- and Behavioral Biology, WWU); STANEWSKY, Ralf (Institute of Neuro- and Behavioral Biology, WWU)

**Vortragende(r):** COCULLA, Angelica (Institute of Neuro- and Behavioral Biology, WWU)



Beitrag ID: 11

Typ: **talk**

## Regulation of microtubule plus-end dynamics in *Drosophila* wing epithelium

*Dienstag, 7. März 2023 15:00 (12 Minuten)*

Microtubules, composed of alpha and beta tubulin heterodimers, are part of the extensive cytoskeleton network in the cell that performs a wide range of activities in different cell and tissue systems. Recently, a focus on the contribution of microtubule-based forces has revealed its role in governing cell and tissue morphogenesis. The patterning of the microtubule array plays a central role in determining the cell's shape. For example, in *Drosophila* wing epithelium, we see a distinct non-centrosomal network of MTs aligned perpendicular to the apico-basal axis along the proximal-distal axis of the wing tissue during tissue remodeling. Previous data from our lab has shown that microtubule alignment is required for cell and tissue elongation during this process. Notably, the increased stability of microtubule plus ends is critical in increasing load-bearing capacity and a potential mechanism contributing to cell shape changes. Here we found that Orbit, the human homolog of CLASP family proteins, plays a key role in regulating the plus end dynamics of apical interphase microtubules at the cell junctions, which might help in the stabilization of microtubules that in turn generate pushing forces required to assist in cell and tissue elongation.

**Hauptautoren:** Frau SARKAR, Sayani (Institute of Cell Biology, ZMBE); Frau THALE, Sameedha (Institute of Cell Biology, ZMBE); Dr. MATIS, Maja (Institute of Cell Biology, ZMBE)

**Vortragende(r):** Frau SARKAR, Sayani (Institute of Cell Biology, ZMBE)

Beitrag ID: 12

Typ: **poster**

## **Modulation of actomyosin-based vertex mechanics controls epithelial permeability**

*Dienstag, 7. März 2023 20:15 (12 Minuten)*

Tricellular junctions (TCJs) at cell vertices are key sites that control paracellular transport as well as passage of migrating cells and pathogens. However, the mechanisms underlying TCJ remodeling are not clear. Here we analyze the roles of actomyosin dynamics during TCJ remodeling in *Drosophila* ovaries, where cell vertices open transiently to allow passage of yolk proteins through the follicle epithelium for uptake by the oocyte. We show that follicle cells comprise a unique organization of actomyosin filaments anchored end-on at TCJs. These structures are rapidly lost and actomyosin contractility is reduced before vertex opening, while F-actin is reassembled at vertices as they close. Consistent with these findings, we show that actin polymerization and myosin II activity are not required for vertex opening, but for closure, whereas stabilizing F-actin or constitutive activation of myosin II are sufficient to prevent vertex opening. Thus, actomyosin-based forces play distinct roles during vertex opening and closure, respectively. Our findings reveal how modulation of actomyosin-based vertex mechanics controls epithelial permeability, providing a framework for elucidating related processes, such as endothelial remodeling during leukocyte extravasation in vertebrates.

**Hauptautoren:** JACOBS, Thea; ISASTI SANCHEZ, Jone; REGER, Steven; LUSCHNIG, Stefan

**Vortragende(r):** JACOBS, Thea

Beitrag ID: 15

Typ: **talk**

## Tissue Interactions During Sensory Neurite Remodeling

*Dienstag, 7. März 2023 17:00 (12 Minuten)*

Neurite pruning and regrowth are conserved developmental processes in which neuronal networks undergo refined changes in connectivity and morphology, which are required for the formation of the adult nervous system. We use *Drosophila* Class 4 dendritic arborization (C4da) neurons to investigate neuronal remodeling, since they eliminate their dendrites by specific degradation (pruning) in early pupal stages and subsequently regrow new adult specific dendritic arbors. But which permissive and/or instructive signals lead to the start of the C4da dendrite regrowth program? C4da neurons extend their dendrites underneath the epidermal layer of the body wall, with epidermal cells undergoing remodeling in a similar timeframe, including the apoptosis of larval epidermal cells (LECs) while adult epidermal cells start proliferating and replace the larval epidermis, leading to massive changes in the tissue environment. Here, we investigate whether epidermis remodeling needs to be finished before C4da dendrite regrowth can actively start, by establishing a live imaging method in which neuronal and epidermal remodeling processes could be visualized simultaneously in a high temporal manner. We also investigate whether impaired epidermal remodeling has an impact on C4da dendrite regrowth by inhibition of larval epidermal cell (LEC) apoptosis. Moreover, we use tissue specific RNAi knockdown of promising candidate genes to identify involved factors in the mechanism activating the dendrite regrowth program. Preliminary results show that active regrowth of C4da neuron dendrites starts after epidermis remodeling is finished and the tissue becomes static again, meaning that tissue movements have mostly subsided, suggesting that these tissue mechanics could inhibit dendrite regrowth. While the inhibition of epidermis remodeling by prevention of LEC apoptosis seems to have negative effects on C4da dendrite regrowth we could also show that the transmembrane receptor Ret might be a key player involved in the dendritic regrowth process.

**Hauptautoren:** KEDING, Lorena; Dr. RUMPF, Sebastian (Institute for Neurobiology)

**Vortragende(r):** KEDING, Lorena

Beitrag ID: 16

Typ: poster

## Brain inflammation triggers macrophage invasion across the blood-brain barrier during pupal stages

*Dienstag, 7. März 2023 19:15 (12 Minuten)*

The central nervous system (CNS) of *Drosophila* can be considered as an immune-privileged organ that is separated from the remaining body by the blood-brain barrier (BBB). This barrier is formed by occluding junctions established between subperineurial glial cells. The BBB prevents the invasion of pathogens and allows ion and metabolite homeostasis. Upon neuronal injury or infection, CNS glial cells are able to respond by phagocytosis. The involvement of external macrophages in CNS injuries and infection was assumed to be impossible due to the formation of the BBB and the inability of macrophages to migrate across this barrier. Here, we present a novel injury model, where glial but not neuronal immunity induction triggers the infiltration of external macrophages into the CNS of *Drosophila*.

First, we tested whether bacterial infection triggers an immune response in the nervous system similar to what is seen in other parts of the animal. Indeed, mRNA analysis showed an activation of the Toll as well as immune deficiency (IMD) pathway together with an upregulation of the PDGF/VEGF-related factor Pvf2. We further demonstrated that induction of the IMD but not of the Toll pathway results in the infiltration of the CNS by macrophages which is mediated through the induction of Pvf2. Transplantation and specific labelling techniques verified that hemolymph-born macrophages invade the CNS. Within the nervous system macrophages are predominantly found in the synaptic neuropil where they phagocytose synapses. We currently study the mechanisms underlying macrophage migration over the BBB and address the balance between detrimental or supportive role of macrophages during CNS immune challenges.

**Hauptautor:** WINKLER, Bente

**Co-Autoren:** FUNKE, Dominik (University of Muenster, Institute for Neurobiology); BENMIMOUN, Billel (Institut Pasteur, Brain plasticity in response to the environment); VEHRING, Leah (Institute for Neurobiology, University of Münster); SPÉDER, Pauline (Institut Pasteur, Brain plasticity in response to the environment); KLÄMBT, Christian

**Vortragende(r):** WINKLER, Bente

Beitrag ID: 17

Typ: **poster**

## Contribution of glial cells during action selection in *Drosophila* larvae

*Dienstag, 7. März 2023 20:30 (12 Minuten)*

Glial cells are required for proper neuronal signalling and homeostasis. In the CNS of *Drosophila* astrocyte-like glia (AG) and cortex glia (CG) modulate neuronal activity (Littleton, Freeman) whereas in the PNs wrapping glia (WG) control neuronal signalling precision (Kottmeier). WG encapsulate either single or bundles of axons along the whole nerve and isolate them from neighbouring axons. Electric field effects around axons, resulting from action potentials, might activate apposed axons, a phenomenon known as ephaptic coupling. This electric cross-talk is prevented by the insulation provided by WG cells which thereby ensure signalling precision. WG specific ablation experiments revealed a decreased neuronal transduction speed and abnormal larval locomotor behaviour. Moreover, uncoordinated muscle contractions were triggered after optogenetic activation of sensory neurons much faster than in wild type, suggesting that ephaptic coupling resulted in unintentional activation of motor axons.

Here, I will present live-imaging approaches to address the question if and where in the PNS ephaptic coupling triggers action potentials in neighbouring axons. For this flies were generated that allow wrapping glia ablation whilst concomitantly activating selected sensory neurons optogenetically and monitoring motor neuron activity via GCaMP8s/ f expression and using mCherry as baseline control (vGlut-GcaMP8s/f, vGlut-mCherry). First results will be discussed.

To address ephaptic coupling in the CNS, I established an assay using optogenetics to activate the Wave or Goro circuit, governing backward crawling or rolling respectively, and taking the behavioural output as readout. First results show that AG ablation is lethal and that blocking of exo-/ endocytosis in AG in the Wave circuit leads to a decrease in backward waves. In contrast, WG ablation does not affect the Wave circuit whilst it has a strong impact on the Goro circuit.

**Hauptautor:** KREBS, Amber Amrei

**Co-Autor:** KLÄMBT, Christian

**Vortragende(r):** KREBS, Amber Amrei

Beitrag ID: 18

Typ: talk

## To identify and characterize novel male infertility associated genes using *Drosophila melanogaster* as a model organism

*Dienstag, 7. März 2023 13:15 (12 Minuten)*

Non-obstructive azoospermia (NOA), defined by the complete lack of spermatozoa in the ejaculate, is clinically the most severe form of male infertility. Despite of this knowledge, the precise cause and molecular diagnosis for the majority of NOA men remains elusive and are diagnosed as 'idiopathic' or unexplained infertility. With advent of next-generation sequencing methods, a continuously increasing number of monogenic causes of male infertility are being discovered at a pace which makes it challenging to validate the functional relevance of the genes for fertility. As such, within this study, I aim to functionally characterize novel human male infertility associated genes that were identified in exome sequencing data of infertile men to reveal the impact of these genes on spermatogenesis using *Drosophila melanogaster*. We identified loss-of-function and rare missense variants in *GLUD2* and *FAM47A* in infertile men. Currently, no functional study or animal model exists to validate the relevance of *GLUD2* and *FAM47A* in human male fertility. Testis-specific knockdown of *GLUD2* orthologue in flies led to infertility due to disrupted individualization complex and empty seminal vesicles without mature sperm. Consistent with the testicular phenotype observed in infertile men –meiotic arrest and sertoli cells only. On the contrary, testis-specific knockdown of *FAM47A* orthologue in flies led to infertility due to loss of germ-cell in the testis which was evident by extremely small testicular size of the testis. Consistent with the sertoli cells only testicular phenotype observed in infertile men with variants in *FAM47A*. Taken together, this study highlights the significance of using *Drosophila melanogaster* as a model organism to investigate functional relevance of novel candidate genes in male fertility.

**Hauptautor:** Dr. GAIKWAD, Avinash (Institute of Reproductive Genetics, University of Münster, Münster, Germany)

**Co-Autoren:** ARAVINA, Mariya; Prof. TÜTTELMANN, Frank (Institute of Reproductive Genetics, University of Münster, Münster, Germany)

**Vortragende(r):** Dr. GAIKWAD, Avinash (Institute of Reproductive Genetics, University of Münster, Münster, Germany)

Beitrag ID: 19

Typ: talk

## Organizing central memory synapses –Nr<sub>x</sub>-1 and glial cells

*Dienstag, 7. März 2023 17:45 (12 Minuten)*

The molecular machinery of synapses, including neurotransmitters and postsynaptic receptor ensemble, are essential for quality and salience of transmitted information; But so is their exact placement along a neuron's arbor. Therefore, locations and numbers are tightly regulated and stereotypic. We showed that such delicately placed synapses are key to general memory computations and integration of aversive and positive extinction memories in *Drosophila*.

Neurexins (Nrxn), transsynaptic molecules, span the synaptic cleft to interact with postsynaptic partners. They organize synaptic interfaces as they guide apposition of presynaptic components with the correct postsynaptic receptors and regulate key components like voltage-gated Ca<sup>2+</sup> channels. Mutations, even single nucleotide exchanges, have been associated with lack of synapses, severe phenotypes, and mental disorders. Nrxns' transsynaptic partners and its role vary depending on the synapse's purpose –e.g. in inhibitory vs. excitatory synapses. Recent research has also shown the involvement of glial Nrxn in clustering postsynaptic glutamate receptors in microdomains. *Drosophila* null-mutants display defects in glutamatergic neuromuscular junction anatomy and function and pan neuronal lack of Nr<sub>x</sub>-1 leads to learning and memory defects. However, the detailed mechanisms through which neuronal and glial Nrxns organize synapses are not well understood across species, particularly on the level of single CNS or GABAergic synapses.

To investigate synapse organization, we use *Drosophila*, because it has one synaptic Nrxn (Nr<sub>x</sub>-1) with nine similar isoforms whereas mammals have three partly redundant Nrxn genes with thousands of diverse isoforms. Additionally, is not only the connectivity of memory neurons and the stereotypic placement of synapses known, but the gene expression and physiology of single neurons can be modified experimentally, too.

We study the anatomical and functional effects of loss of Nr<sub>x</sub>-1 as well as single nucleotide mutations induced via CRISPR-Cas9, that have been associated with mental disorders in patients. Thereby, focusing on a defined number of GABAergic CNS synapses between two neurons essential for the extinction of aversive- and expression of other memories. Anatomical parameters will be assessed with t-GRASP and electron microscopy, behaviour with learning and memory paradigms. The roles of different parts of the presynaptic machinery, transsynaptic partners and glial Nr<sub>x</sub>-1 function are studied with a knock down screen.

**Hauptautoren:** Dr. OTTO, Nils (Institute for Anatomy and Molecular Neurobiology & CNCB, University of Oxford); Dr. REISSNER, Carsten (Institute for Anatomy and Molecular Neurobiology); Prof. WADDELL, Scott (CNCB, University of Oxford); Prof. MISSLER, Markus (Institute for Anatomy and Molecular Neurobiology)

**Vortragende(r):** Dr. OTTO, Nils (Institute for Anatomy and Molecular Neurobiology & CNCB, University of Oxford)

Beitrag ID: 20

Typ: **talk**

## **Drosophila as a model to study glomerular disease**

*Dienstag, 7. März 2023 15:45 (12 Minuten)*

T.B.A.

**Hauptautor:** Dr. GEORGE, Britta (Molekulare Nephrologie)

**Vortragende(r):** Dr. GEORGE, Britta (Molekulare Nephrologie)



Beitrag ID: 21

Typ: **talk**

## **The making and breaking of tricellular contacts in epithelial tissues**

*Dienstag, 7. März 2023 15:15 (12 Minuten)*

T.B.A.

**Hauptautor:** SCHLEUTKER, Raphael (AG Luschnig, Formation of Epithelial Tubes)

**Vortragende(r):** SCHLEUTKER, Raphael (AG Luschnig, Formation of Epithelial Tubes)

Beitrag ID: 22

Typ: **talk**

## **Modelling cell polarity and cell proliferation control in Drosophila**

*Dienstag, 7. März 2023 15:30 (12 Minuten)*

T.B.A.

**Hauptautor:** Prof. KRAHN, Michael (Medizinische Zellbiologie, Medizinische Klinik D, UKM)

**Vortragende(r):** Prof. KRAHN, Michael (Medizinische Zellbiologie, Medizinische Klinik D, UKM)

Beitrag ID: 23

Typ: **poster**

## A fair place for your data - practical guide for easy and efficient image data and meta data management

*Dienstag, 7. März 2023 21:00 (12 Minuten)*

In life sciences, light microscopy imaging systems are key instruments for various research areas as they are capable to record multidimensional data delivering major insights into the biology of molecules, cells, and whole organisms. The generated data shows a high diversity in terms of content and size, and is saved in a myriad of proprietary file formats [1]. To quantitatively and qualitatively analyze this data, high demands are set on the technical infrastructure. In addition, data should be stored according to the FAIR criteria ensuring the data is findable, accessible, interoperable and reusable [2]. The implementation of the FAIR criteria is strongly supported by national and international research organizations, e.g., the German Research Foundation. To make data reusable and reproducible, convenient options for sharing large, original datasets need to be offered [3]. Especially when sharing data, the annotation of the data with meaningful metadata is an essential prerequisite to enable reproduction of results and reuse of the data for new studies. The required metadata concerns different aspects, such as technical metadata about microscope configurations during image acquisition (e.g., laser lines & detector settings), or experimental metadata (e.g., fluorescent proteins, antibodies & fixation methods). Several consortia have published guidelines about metadata for biological images to advance quality assessment and reproducibility [4,5]. The aforementioned challenges of the various proprietary file formats, the ever-increasing amount of data and the need to enrich microscopy data with metadata confront scientists with challenges that cannot be met without well planned concepts for data management. Ideally, the concepts should ease working with the generated imaging data on a daily basis. One of the most important tools for this is the microscopy image data management system OMERO [6].

**Hauptautoren:** WEISER, Sarah (Münster Imaging Network); WENDT, Jens (Münster Imaging Network); ZOBEL, Thomas (Münster Imaging Network)

**Vortragende(r):** WEISER, Sarah (Münster Imaging Network)

Beitrag ID: 24

Typ: talk

## Drosophila melanogaster as a model organism for motile ciliopathies

Dienstag, 7. März 2023 13:30 (12 Minuten)

Motile ciliopathies are a heterogeneous group of genetic disorders caused by dysfunction of motile cilia in various organ systems. A common motile ciliopathy is the multisystem disorder primary ciliary dyskinesia, characterized by recurrent respiratory symptoms. Motile ciliopathies also play an important role in the etiology of male infertility, as sperm flagella defects often occur in combination with structural and functional abnormalities of other types of motile cilia. However, to date, a genetic cause of male infertility can only be found in 4.3% of cases leaving a large proportion of diagnoses incomplete. In addition, 20-30% of PCD cases are still genetically unsolved. Therefore, it is necessary to further elucidate the genetic landscape and functionally characterize genetic defects associated with motile ciliopathies and male infertility. The fruit fly *Drosophila melanogaster* is recently emerging as a model organism for motile cilia biology. Although in *Drosophila* only two specialized cell types carry motile cilia: the sperm flagellum with a 9+2 axoneme and the ciliated dendrite of auditory/proprioceptive (chordotonal, Ch) neurons with a 9+0 axoneme, it has been found that molecules essential for cilia motility are well conserved. They present with restricted cell type-specific expression patterns and phenotypes. These differences may reflect specialized functions for motility in the two cilia types. Furthermore, around 61% of *Drosophila* genes are conserved in humans and 59% of human disease genes are homologous in the fly. As *Drosophila* represents a suitable, ethical and high-throughput alternative for testing and functional characterization of candidate genes, we here propose an RNAi silencing approach of candidate genes in the fruit fly to improve our understanding of the underlying genetic causes of motile ciliopathies, including male infertility.

**Hauptautor:** APREA, Isabella (University Clinics Muenster, Department of General Pediatrics)

**Co-Autoren:** WILKEN, Alina (University Clinics Muenster, Department of General Pediatrics); OM-RAN, Heymut (University Clinics Muenster, Department of General Pediatrics)

**Vortragende(r):** APREA, Isabella (University Clinics Muenster, Department of General Pediatrics)

Beitrag ID: 25

Typ: **talk**

## **Münster Imaging Network from acquisition to analysis and publication - An overview**

*Dienstag, 7. März 2023 14:45 (12 Minuten)*

T.B.A.

**Hauptautor:** Dr. ZOBEL, Thomas (Münster Imaging Network)

**Vortragende(r):** Dr. ZOBEL, Thomas (Münster Imaging Network)

Beitrag ID: 26

Typ: **poster**

## **ATF4-CHOP signaling in OSGEP-related pathogenesis in podocytes and drosophila nephrocytes**

*Dienstag, 7. März 2023 19:00 (12 Minuten)*

Recessive mutations in the gene OSGEP cause Galloway-Mowat syndrome, defined by developmental brain defects and progressive glomerulosclerosis in paediatric patients. OSGEP is part of a multiprotein complex that catalyzes post-transcriptional modifications of tRNA and thereby regulates protein translation. Previous studies reported an accumulation of endoplasmic reticulum stress following OSGEP depletion; however, the exact molecular mechanisms of podocyte injury in this condition remain elusive.

**Hauptautoren:** Dr. KRAUSEL, Vanessa (Universitätsklinikum Münster, Medizinische Klinik D); PUND, Lisanne (Universitätsklinikum Münster, Medizinische Klinik D); WEIDE, Thomas (Universitätsklinikum Münster, Medizinische Klinik D); Prof. PAVENSTÄDT, Hermann (Universitätsklinikum Münster, Medizinische Klinik D); Prof. KRAHN, Michael (Universitätsklinikum Münster, Medizinische Klinik D); Dr. BRAUN, Daniela (Universitätsklinikum Münster, Medizinische Klinik D)

**Vortragende(r):** Dr. KRAUSEL, Vanessa (Universitätsklinikum Münster, Medizinische Klinik D)

Beitrag ID: 27

Typ: poster

## Regulation of microtubule mechanics during epithelial morphogenesis

Dienstag, 7. März 2023 20:45 (12 Minuten)

Coordinated rearrangements of cytoskeletal structures govern cell and tissue morphogenesis. In contrast to actin-based forces, our knowledge of microtubule (MT)-based forces is still limited. In recent years, we have shown that the Ft-PCP signaling pathway globally patterns the MT cytoskeleton to coordinate local cell behavior during *Drosophila* wing morphogenesis. Interestingly, in *ft-PCP* mutant animals, where MT alignment is disrupted, cells and tissue fail to elongate, suggesting an interdependence of these processes. Furthermore, we have shown that physical forces based on the global patterning of MTs contribute to cell mechanics. However, the mechanisms regulating MT organization and patterning during tissue remodeling are not understood. We recently showed that the formation of non-centrosomal MTs in wing cells depends on MT minus-end binding protein Patronin (CAMSAP in vertebrates). Consistently, depletion of Patronin leads to cell and tissue elongation defects.

Importantly, MT-based mechanical properties should be adaptable to environmental forces that vary considerably across tissue types to be functionally appropriate. Strikingly, our analysis revealed that non-centrosomal MTs in wing cells have a mean diameter of 29 nm, substantially larger than the diameter of canonical 13 protofilament MTs (~25nm). This is significant because the increased diameter of the tubular architecture caused by the increased number of protofilaments dramatically increases flexural rigidity, thus providing an alternative mechanism for cells to regulate MT stiffness and adapt to cell mechanics. Furthermore, as the formation of non-centrosomal MTs in wing cells depends on Patronin, our data suggest that Patronin regulates MT lattice diameter by regulating the number of MT protofilaments. Together, these results provide the molecular basis to explain how regulating MT properties and organization controls cell mechanics during tissue remodeling.

**Hauptautoren:** THALE, Sameedha (Institute of Cell Biology, ZMBE); SARKAR, Sayani (Institute of Cell Biology, ZMBE); Dr. MATIS, Maja (Institute of Cell Biology, ZMBE)

**Vortragende(r):** THALE, Sameedha (Institute of Cell Biology, ZMBE)