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# 2024 FALL SEMINAR SERIES


## Svenja Illien-Junger, Ph.D.

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**Department of Orthopaedics, Atlanta, GA**


**THURSDAY October 31, 2024**
**11am-12pm**
**PWEB 150**

## ABSTRACT:


***PHLPPing the switch: PHLPP inhibitors to promote intervertebral disc health***

Back pain is a leading cause of global disability and is strongly associated with intervertebral disc (IVD) degeneration. The causes of IVD degeneration is multifactorial, including genetic predisposition, aging, mechanical stress and trauma. With aging and degeneration, cell loss and transformation occur, resulting in a chronic inflammatory environment, a fibrotic phenotype, and decreased production of matrix. It has been shown that the phosphatase PH domain leucine rich repeat protein phosphatase-1 (PHLPP1) is correlated with inflammation and matrix degradation in several musculoskeletal tissues. Our lab demonstrated that PHLPP1 expression was increased in degenerated human IVDs, suggesting a role of PHLPP1 in spontaneous IDD. To elaborate the association between PHLPP1 and IDD, we used an age-related spontaneous IVD degeneration mouse model. We demonstrated that Phlpp1 deficiency delayed IVD degeneration in mice by promoting matrix synthesis and inhibiting apoptosis. To evaluate if Phlpp1 deficiency has the potential to promote IVD healing, we used a surgical-induced IVD degeneration mouse model, we found that Phlpp1 deficiency promoted IVD healing by cell promoting survival and matrix production. Small-molecule PHLPP inhibitors NSC117079 and NSC45586 have been shown to inhibit PHLPP in several cell types, but their efficiency varied between tissues. To evaluate their efficacy against IVD degeneration, we tested the efficacy of each inhibitor to promote a healthy NP cell phenotype in ex-vivo mouse IVD organ cultures and in vitro cultures with degenerated human NP cells. Our results indicated that only treatment with NSC45586 prevented shrinkage of the notochordal band. Similarly, Keratin-19, a marker for a healthy NP phenotype, was only increased after NSC45586 treatment. In vitro, only NSC45586 treatment promoted NP cell viability, Keratin19 expression and matrix metabolism. The Inhibitor NSC117079 did not show significant alterations in any of the measured parameters. Together, our findings suggest that PHLPP1 deficiency slows down aging induced spontaneous aging and decelerates IVD degeneration after injury. The small molecule inhibitor NSC45586 may act as a therapeutic target to inhibit PHLPP1 and promote NP cell health.



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## BIOGRAPHY:

Dr. Illien-Junger is an Assistant Professor at the Emory University School of Medicine. Their research focus is on intervertebral disc research, specifically addressing the roles of injury, nutrition, and mechanical loading on disc degeneration and repair. Dr. Illien-Junger has solid proficiency in the studies of intervertebral disc aging and injury related degenerative disc diseases from a cellular, molecular, and biomechanical perspectives. Their laboratory was the first to establish that PHLPP contributes to the progression of intervertebral disc degeneration.

Dr. Illien-Junger is originally from Germany, and received their PhD at the AO Research Institute, in Davos, Switzerland. Before accepting the Assistant Professor position at Emory, they were at the Mount Sinai School of Medicine, first as a postdoc and later as Assistant Professor.

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For questions, please contact Dr. Sina Shahbazmohamadi sina@uconn.edu or Sarah Dunnack sarah.dunnack@uconn.edu