

MMI 291 Seminar Series

Current Theme: Interdisciplinary Research
Fall Quarter 2022 – CRN 41473

Friday Seminar – 12:10-1 p.m. (Zoom)

“Neuroinfections: Resolving mechanisms of fungal translocation from blood-to-brain”

Research

Angie Gelli, Ph.D., is a Professor in the Department of Pharmacology in the School of Medicine at UC Davis where she has been a faculty member since 2003. Born and raised in Canada, Dr. Gelli received her B.Sc. and Ph.D. from the University of Toronto and was an NSERC (Natural Sciences and Engineering Research Council of Canada) Postdoctoral Scholar at Mount Sinai Hospital. Dr. Gelli's lab investigates host-pathogen interactions in fungal neuroinfections to resolve mechanisms mediating pathogen interactions with the blood-brain barrier (BBB). Fungal infections of the central nervous system (CNS) are understudied despite the high mortality and persistent threat of multi-drug resistant neuroinfections. Her lab was the first to generate assays that leveraged *in vitro* models of the BBB and *in vivo* models of fungal pathogenesis to identify mechanisms of fungal translocation across the BBB, and new potential therapeutic targets. Dr. Gelli's research led to a patent and a prestigious research award from The Hartwell Foundation that served as a springboard for her current research on mechanisms of BBB dysfunction in aging, dementia and chemical exposure. Dr. Gelli's research is supported by NIH (NINDS, NIAID), NSF, The Hartwell Foundation and CFAR.

Seminar

Fungal infections of the CNS have the highest morbidity and mortality when compared to other causative agents of CNS infections. *Cryptococcus neoformans* (*Cn*) is the most common cause of adult brain infection resulting in a chronic instead of an acute or subacute meningoencephalitis. We are investigating molecular mechanisms promoting the translocation of fungi from blood-to-brain while also identifying the structural and molecular changes in the neurovascular unit - i.e., the blood-brain barrier - and how that informs neurological changes in the brain. Using transcriptomics analysis, we identified a receptor tyrosine kinase (EphA2) as a key player in BBB dysfunction and we propose that *Cn* penetrates the BBB by engaging EphA2 which creates a binary path into the CNS. In addition to identifying therapeutic targets to prevent fungal meningoencephalitis, we are using the OBOC (one-bead, one compound) technology to identify novel peptides with broad antifungal activity.

Publications

¹Aaron PA, Jamklang M, Uhrig JP, **Gelli A.** (2018) The blood-brain barrier internalizes *Cryptococcus neoformans* via the EphA2-tyrosine kinase receptor. *Cell. Micro.* 20(3).²Most highly cited article for the journal in 2018.

Bansal S*, Vu K*, Ruiwu Liu, Ajena Y, Xiao W, Menon S, Bennett A, **Gelli A**, Lam KS. (2022) Discovery of a potent antifungal peptide through OBOC combinatorial library screening. *ACS Infect. Dis. Disease, J of American Chemistry Society*. *Equal contribution

October
28



Angela Gelli, Ph.D.
Professor
Pharmacology
University of California, Davis

**October 28, 2022
12:10 – 1 p.m.
ZOOM Meeting**

Medical Microbiology &
Immunology
School of Medicine

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We hope to see you there!