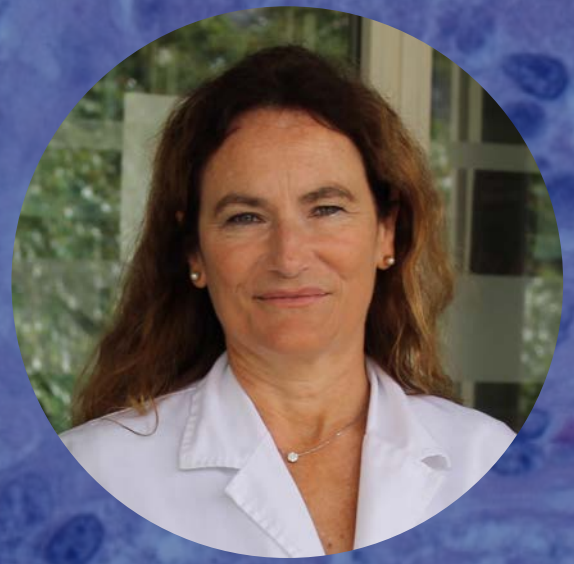
PIONEERS IN BIOMEDICAL RESEARCH SEMINAR

Presented by the Fralin Biomedical Research Institute at VTC and co-sponsored by the institute's Cancer Research Group



ARANTXA TABERNERO, Ph.D.

Professor of Biochemistry and Molecular Biology
Institute of Neuroscience Castilla y León
University of Salamanca
Spain

Virtual Seminar: Src Inhibitory Peptides Based on Connexin43 as a Promising Therapy Against Glioblastoma

Glioblastomas are the most frequent primary brain tumors and remain among the most incurable cancers. Connexin43 (Cx43), the main constituent of gap junctions, has been traditionally considered a tumor suppressor protein in glioblastoma; however, Cx43 can also play pro-tumorigenic roles, suggesting that very specific tools should be used to mimic specifically the antitumor effects of Cx43. The C-terminal domain of Cx43 interacts with a plethora of molecules and acts as an intracellular signaling hub. This is the case for the proto-oncoprotein c-Src, which is recruited by Cx43 together with its inhibitors CSK and PTEN. This interaction causes the inhibition of c-Src and its downstream oncogenic pathways. Dr. Tabernero designed a cell-penetrating peptide, TAT-$Cx43_{266-283}$, that recapitulates the inhibition of c-Src by Cx43. Malignant gliomas have high oncogenic c-Src activity; moreover, cancer stem cells, including glioblastoma stem cells (GSCs), rely on the activity of this oncoprotein for metabolic reprogramming, survival, stemness, and invasion. Importantly, TAT-$Cx43_{266-283}$ inhibits c-Src activity and consequently exerts potent antitumor effects specifically in glioblastoma cells without affecting healthy brain cells, such as neurons and astrocytes. In brief, Tabernero found that TAT-$Cx43_{266-283}$ reduces migration, invasion, metabolic plasticity and survival in mice and human GSCs, including freshly removed surgical specimens studied as undissociated glioblastoma blocks. Moreover, TAT-$Cx43_{266-283}$ inhibits c-Src, impairs malignant growth, and enhances survival in mouse models in vivo, without exerting toxicity in endogenous brain cells, supporting the translational potential of this peptide for the treatment of glioblastoma.

FRIDAY, OCT. 1 at 11:00 a.m.

Watch live via Zoom at https://virginiatech.zoom.us/j/82722436593 or at https://fbri.vtc.vt.edu/events/live-webcast.html.

FRALIN BIOMEDICAL RESEARCH INSTITUTE AT VTC
VIRGINIA TECH