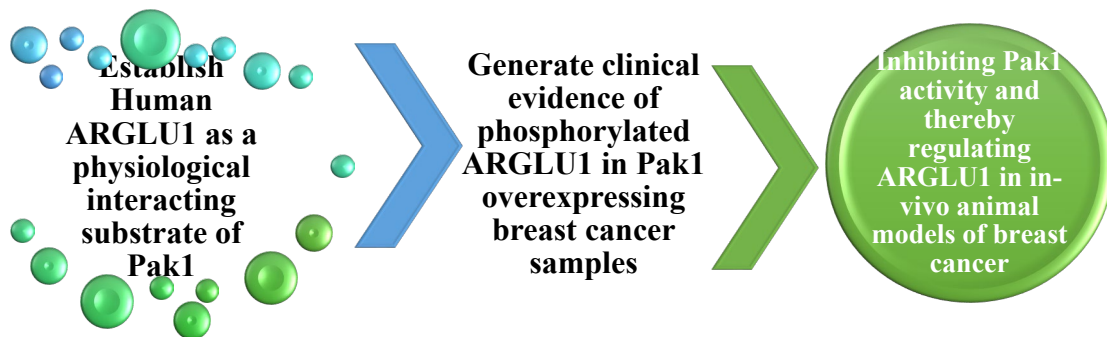# Phosphorylation-dependent regulation of Arginine and Glutamine-rich protein 1 (ARGLU1) by P21 activated kinase 1 (Pak1) -a regulatable molecular switch with therapeutic potential in breast cancer

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Department of Science and Technology-Science and Engineering Research Board (DST-SERB)

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SERB-CRG

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Rs. 52,32,120

Duration of the Project (years)
3

Graphical Abstract/ Layout

Establish Human ARGLU1 as a physiological interacting substrate of Pak1

Generate clinical evidence of phosphorylated ARGLU1 in Pak1 overexpressing breast cancer samples

Inhibiting Pak1 activity and thereby regulating ARGLU1 in in-vivo animal models of breast cancer

Project Description:

Arginine and Glutamine-rich protein 1 (ARGLU1) and p21-activated kinase 1 (Pak1) are frequently overexpressed in breast tumors, contributing to aggressive phenotypes and unfavorable clinical outcomes. 17-β estradiol (E2) activates estrogen receptor α (ERα), which plays a key role in breast tumorigenesis. ARGLU1 is crucial for estrogen receptor-mediated gene transcription and breast cancer cell growth, making it a promising therapeutic target for breast cancer treatment.

Based on preliminary data, we propose that inhibiting both ARGLU1 and Pak1 may be a novel treatment strategy for breast cancer. Our in silico findings indicate that Pak1 phosphorylates ARGLU1; This phosphorylation could act as a molecular switch, regulating ARGLU1 activity and its plausible role in Estrogen dependent cancers. We intend to systematically investigate the effects of Pak1-mediated post-translational modification of ARGLU1 and find ways to inhibit it.

We hypothesize that targeting Pak1 kinase activity could regulate ARGLU1, offering a new therapeutic approach. Our goals are to establish ARGLU1 as a Pak1 substrate, generate clinical evidence of phosphorylated ARGLU1 in Pak1-overexpressing breast cancer, and evaluate the effects of Pak1 inhibition in vivo.

Products/ Instruments/ Results/ Outreach Activities (Pictures)

Establish Pak1 as the upstream regulator of ARGLU1.

Combination of Pak1 inhibitors and ARGLU1 inhibitor could be tested out for therapeutic value

Sponsored Research and Industrial Consultancy (SpoRIC)