Guest lecture

"Understanding the role of estrogen receptor in breast cancer"

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10 AM in the BMB seminar room

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Abstract: Estrogen Receptor (ER) is the defining feature of luminal breast cancer. ER requires associated proteins to interact with the DNA, including FoxA1 and GATA3. GATA3 and FoxA1 are mutated in primary breast cancer and ESR1 (ER) is mutated in the metastatic context. Interestingly, GATA3 mutations, which occur in ~14% of ER+ cases, tend to cluster into two classes, one of which are C-terminal frame shift mutations, commonly resulting in an elongated GATA3 protein. We have explored the potential role of these elongating GATA3 mutations, by engineering the mutation into a cancer cell line and characterizing the impact of this common mutational event on ER biology.

It is well established that most ER+ breast cancer also express Progesterone Receptor (PR) and Androgen Receptor (AR). Several labs, including ours, have recently implicated molecular cross-talk between PR/AR and the ER pathway, providing the opportunity for exploiting parallel hormonal pathways for therapeutic benefit. However, there are contradictory findings associated with the role of PR and progestogens in breast cancer and inappropriate extrapolations made from normal mammary gland biology to cancer contexts. To address this and to fully exploit the hormonal cross-talk, we have extended on our initial observations to characterize the nuclear receptor cross-talk in cancer models and primary tumour explant samples and to compare distinct PR ligands that have traditionally been linked with different physiological outcomes. In addition, we have initiated a clinical trial to explore the therapeutic potential of repurposing PR agonists for primary ER+ breast cancer.

Host: Professor Susanne Mandrup, Department of Biochemistry and Molecular Biology, SDU.