Welcome to the 5th FICAN seminar

Thursday 20.04.2023 at 15-16

Topic: Inherited breast cancer susceptibility - Identification of novel factors using Northern Finnish breast cancer cohorts

This time the seminar is organized by FICAN North. The seminar will be held online (Microsoft Teams) and is open to everyone interested in cancer research.

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Speaker

Katri Pylkäs

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Abstract

Our research focuses on breast cancer genetics and inherited predisposition to this common disease. Based on the familial clustering of breast cancer, up to 10% of all cases is estimated to be caused by strong inherited predisposition. However, the known predisposing alleles explain less than half of the hereditary component,leaving the causal factors for majority of breast cancer families unknown. Our research aims for the identification of additional inherited predisposing alleles and understanding their effect on disease onset and behavior. Our studies are based on large breast cancer cohorts collected from Northern Finland together with the clinical collaborators. The predisposing genetic variants are searched by using various genomic approaches, addressing both nucleotide level variation and larger scale genomic events. For the functional characterization of the identified alleles, we use functional genomics, biochemical and disease modelling approaches. For example, we have identified several predisposing founder alleles in Northern Finnish population, including MCPH1 c.904_916del (p.Arg304ValfsTer3), SERPINA3c.918-1G>C and ATM c.7570G>C (p.Ala2524Pro). Of these, MCPH1 and SERPINA3 variants are categorized as moderate-risk alleles, whereas ATM variant is defined as a high-risk allele, and the carriers are counselled and monitored accordingly. In our research projects, we will utilize new genomic methods, the latest being optical genome mapping technology, which has been set-up into our laboratory. These are also offered as a service for other research groups and routine clinical diagnostics.

Relevant references for this talk:

- Kankuri-Tammilehto M, Tervasmäki A, Kraatari-Tiri M, Rahikkala E, Pylkäs K, Kuismin O. ATM c.7570G>C is a high-risk allele for breast cancer. Int J Cancer. 2023 Feb 1;152(3):429-435. doi: 10.1002/ijc.34305.
- Koivuluoma S, Tervasmäki A, Kauppila S, Winqvist R, Kumpula T, Kuismin O, Moilanen J, Pylkäs K. Exome sequencing identifies a recurrent variant in SERPINA3 associating with hereditary susceptibility to breast cancer. Eur J Cancer. 2021 Jan;143:46-51. doi: 10.1016/j.ejca.2020.10.033.
- Mantere T, Winqvist R, Kauppila S, Grip M, Jukkola-Vuorinen A, Tervasmäki A, Rapakko K, Pylkäs K. Targeted Next-Generation Sequencing Identifies a Recurrent Mutation in MCPH1 Associating with Hereditary Breast Cancer Susceptibility. PLoS Genet. 2016 Jan 28;12(1):e1005816. doi: 10.1371/journal.pgen.1005816.
- Tervasmäki A, Mantere T, Eshraghi L, Laurila N, Tuppurainen H, Ronkainen VP, Koivuluoma S, Devarajan R, Peltoketo H, Pylkäs K. Tumor suppressor MCPH1 regulates gene expression profiles related to malignant conversion and chromosomal assembly. Int J Cancer. 2019 Oct 15;145(8):2070-2081. doi: 10.1002/ijc.32234.

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