

6TH WORLD FORUM ON BREAST AND CERVICAL CANCER



Michal Linial

Dept of Biological Chemistry, The Hebrew University of
Jerusalem, Jerusalem, Israel

Discovering hereditary breast cancer genes from families and large population

Understanding inherited genetic risk is essential for advancing early detection, prevention, and personalized treatment of breast cancer (BC). While several breast cancer risk loci such as BRCA1/2 have been identified, their biological mechanisms often remain unclear. For discovery of cancer predisposition genes (CPG) and to improve interpretability, we analyzed BC predisposition in the UK Biobank (UKB) using a gene-based approach called proteome-wide association studies (PWAS), which links germline variants to protein function. PWAS identified both known and novel genes that were significantly associated with BC risk, including genes showing protective effects, where damaging variants were linked to reduced risk. Combined with GWAS, we uncovered several novel risk loci and highlighted the importance of recessive inheritance. Furthermore, we revisiting exome sequences from BC-affected members belonging to over 30 families and identified BC-associated candidate genes, most of which were associated with a specific family origin and highlighted the interference with regulation of immunity and DNA damage. The combined approaches provide a nuanced view of BC genetics and offers new opportunities for early diagnosis, risk prediction, and personalized care. Read more in: (i) Brandes, N. et al. (2021) Scientific reports 11, 14901; (ii) Passi, G., et al. (2024) Briefings in Bioinformatics 25 (4), bbae346.

Biography

Prof. Michal Linial is a leading expert in computational biology and bioinformatics at the Hebrew University of Jerusalem. She directs both experimental and computational research focused on protein evolution, neurobiology, and disease mechanisms. A former director of the Israel Institute for Advanced Studies and head of ELIXIR-Israel, she has published over 150 peer-reviewed articles. Linial is an elected Fellow of the ISCB and has developed key bioinformatics tools like ProtoNet and PANDORA. Her work bridges molecular biology with cutting-edge data science and machine learning.