Rachael Natrajan, J Stem Cell Res Ther 2015, 5:7
http://dx.doi.org/10.4172/2157-7633.S1.014

OMICS International
conferenceseries.com

4th International Conference and Exhibition on
Cell & Gene Therapy

August 10-12, 2015 London, UK

# Targeting low frequency mutations in breast cancer

**Rachael Natrajan**
The Institute of Cancer Research, UK

The advent of next generation sequencing has identified a plethora of alterations associated with different subtypes of breast cancer. However the bottleneck is identifying which of these alterations are driving tumor growths, particularly those that are present at low frequency. To address this, we have taken an integrative approach to identify driver alterations that can be exploited as therapeutic targets, by i) identifying alterations at higher frequency in rare subtypes of breast cancer and ii) integrating high-throughput functional genomic screen data to identify genes that are selectively dependent in cancer cells as evidence of functionality. These analyses have identified recurrent mutations in SF3B1, a component of the spliceosome to be significantly associated with ER-positive disease, and in particular 16% and 6% of papillary and mucinous carcinomas of the breast. RNA sequencing identified a conserved set of differentially spliced events expressed in tumours with SF3B1 mutations. Moreover, SF3B1 mutant cell lines were found to be sensitive to the SF3b complex inhibitor spliceostatin A and treatment resulted in perturbation of the splicing signature. In addition, integration of functional genomics screen data identified recurrent CDK12 mutations and inactivating fusion genes associated with different breast cancer subtypes that lead to loss of CDK12 protein and loss of competent DNA repair, and consequent sensitivity to PARP inhibitors. Our findings indicate that rare genomic alterations in breast cancer may constitute bona-fide drivers and novel therapeutic targets.

## Biography

Rachael Natrajan completed her PhD and Postdoctoral studies from The Institute of Cancer Research focusing on the molecular pathology of pediatric and breast cancers. She now leads her own team looking at the functional characterization of high-throughput genomic profiling data and the translation of these as novel therapeutic targets in breast cancer.

## Notes: