✉ **CONTACT:** Emeritus Professor Irena Cosic irenacosic@me.com

Analysis of BRCA-1 Mutations Using the Resonant Recognition Model

Irena Cosic, Drasko Cosic and Katarina Lazar
AMALNA Consulting, Black Rock, Australia
amalnaconsulting.com
email: irenacosic@me.com

Background

The number of mutations within the BRCA-1 gene are related to development of breast cancer, ovarian cancer, as well as prostate cancer and pancreatic cancer.

We have analysed BRCA-1 function and functional mutations using our previously developed Resonant Recognition Model (RRM), which is capable to analyse protein biological functions/interactions, predict bioactive mutations and design *de novo* bioactive peptides.

BRCA-1 Protein

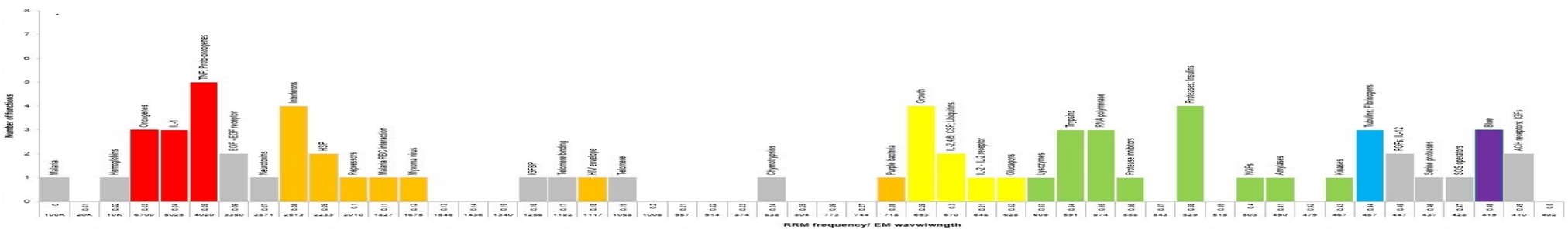
BRCA-1 protein is involved in DNA repair.

Certain variations of BRCA-1 protein lead to increased risk of breast cancer, ovarian cancer, prostate cancer and pancreatic cancer.

Mutations in BRCA-1 proteins are found to be inherited and are ethnic specific. These mutations have been spread all along the BRCA-1 protein sequence, but with most of them clustered between amino acids in ranges of: 460-555, 800-960, 1020-1220 and 1660-1840.

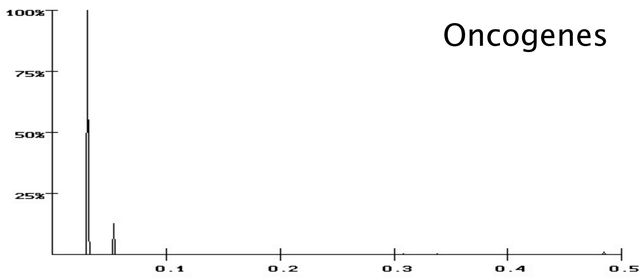
Methods – Resonant Recognition Model (RRM)

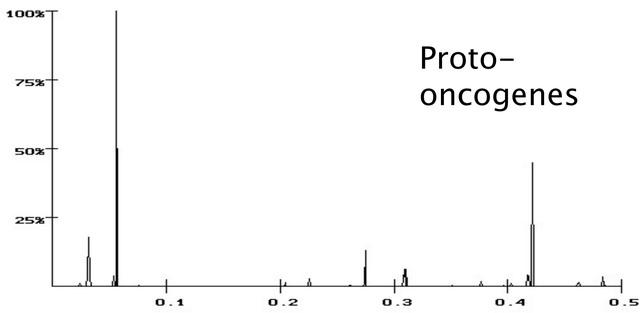
The RRM is physico-mathematical model, which is capable to analyse protein biological functions/interactions, predict bioactive mutations and design de novo bioactive peptides with desired biological function. The RRM model is based on findings that certain periodicities within the distribution of energies of free electrons along the protein are strongly correlated with the protein biological functions/interactions. The spectrum of biological functions/interactions, as determined so far, versus RRM frequencies is presented below:



Oncogene Vs Proto-Oncogene

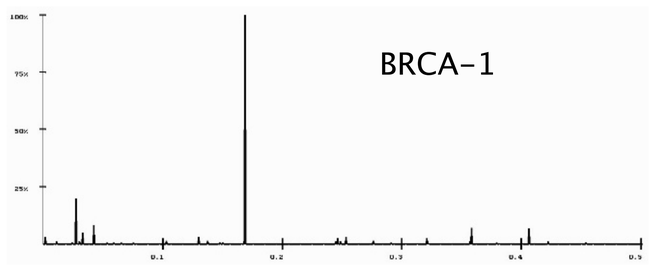
The RRM analysis of oncogene proteins, which are involved in oncogene transformation of the cell, have shown the most prominent characteristic at frequency of 0.0322, with less prominent characteristic at frequency of 0.0537. The RRM analysis of proto-oncogene proteins, which are very homologous to oncogene proteins, but are not producing cell transformation, have shown the most prominent characteristic frequency of 0.0537, with less prominent characteristic at frequency of 0.0322. The conclusion of this earlier work was that frequency of 0.0322 characterise process of cell transformation, while frequency of 0.0537 characterise cell growth without transformation.





Prediction of BRCA-1 Critical Mutations

When nine BRCA-1 proteins from different species were compared, the common characteristic frequency was found to be at 0.1685. This frequency could be characteristic of DNA repair function of BRCA-1.



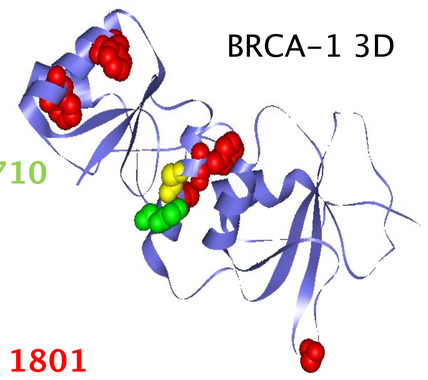
The second prominent frequency common for all analysed BRCA-1 proteins is overlapping with previously identified oncogene frequency. Thus, we identified two distinct RRM characteristics within the BRCA-1 proteins, one related to cell transformation and the other related to DNA repair. Based on these characteristics, we propose related functional mutations in human BRCA-1 protein (P38398).

The six most significant functional mutations related to oncogene frequency are at positions:

57, 1232, 1492, 1706, 1709 and 1710

The six most significant functional mutations related to DNA repair frequency are at positions:

1662, 1668, 1704, 1706, 1748 and 1801



Our findings show that majority of predicted functional mutations related to both oncogene and DNA repair functions are within region experimentally found to be DNA binding region between sequence positions 1646 and 1859. Specifically, we propose that:

- the region between sequence positions 1704 and 1710 is related to both oncogene and DNA repair functions;
- the region between sequence positions 1232 and 1492 is predominantly related to oncogene function;
- the region between sequence positions 1662 and 1668 is predominantly related to DNA repair function.

All predicted functional mutations are positioned within the 3D structure of BRCA-1 DNA binding segment and highlighted with CPKs as presented in the 3D figure above.

Discussion

Majority of mutations in BRCA-1 found to be related to breast cancer are in the region between positions 1685 and 1804, which is related to our prediction for both oncogene and DNA repair functions.

The mutations related to both ovarian cancer and breast cancer are in the region between positions 1187 and 1243, which is more related to oncogene function.

References

1. Cosic I. Macromolecular bioactivity: is it resonant interaction between macromolecules? –Theory and applications, *IEEE Trans. on Biomedical Engineering*, 1994, 41, 1101-1114.
2. Cosic I. Virtual spectroscopy for fun and profit, *Biotechnology*, 1995, 13, 236-238.
3. Cosic I. The Resonant Recognition Model of Macromolecular Bioactivity: Theory and Applications, *Birkhauser Verlag, Basel*, 1997.
4. Cosic I, Cosic D, Lazar K. Analysis of Tumor Necrosis Factor Function Using the Resonant Recognition Model, *Cell Biochemistry and Biophysics*, 2016, 74(2), 175-180, doi: 10.1007/s12013-015-0716-3.

T +1.714.463.4673 18340 Yorba Linda Blvd. Ste 107
F +1.714.970.2173 PMB 427, Yorba Linda, CA 92886
info@labroots.com • labroots.com