

5th International Conference on

GLYCOBIOLOGY & GLYCOPROTEOMICS

&

3rd International Conference on

MOLECULAR BIOLOGY & NUCLEIC ACIDS

August 27-28, 2018 | Toronto, Canada

DNA recognition by the *BRCA1* tumor suppressor

Ann J Fuelle, Zhouling He, and Colin G Wu
Oakland University, USA

Statement of the Problem: Human *BRCA1* encodes a tumor suppressor protein that repairs double-stranded DNA breaks in cells. Mutations in *BRCA1* are closely linked to the early onset of breast and ovarian cancers. *BRCA1* protein participates in several DNA repair pathways but the molecular mechanisms through which *BRCA1* targets damaged DNA structures is not well-understood.

Methodology & Theoretical Orientation: A detailed comparison of the DNA binding preferences of *BRCA1* was performed on its DNA binding domains (DBD1 aa330-554, DBD2a aa894-1057, DBD2b aa936-1057, and BRCT aa1745-1861). Each *BRCA1* fragment was expressed in *E. coli* and purified from other proteins using nickel affinity and heparin ion exchange chromatography. The relative affinities of these purified *BRCA1* domains for various DNA targets (ssDNA, dsDNA, human G4 telomere, etc.) were measured by biolayer interferometry (BLI) as well as fluorescence spectroscopy. These equilibrium constant values were used to rank order the DNA binding preferences for each protein domain.

Findings: We find that DBD1 has the highest affinity for dsDNA. Both DBD2a and DBD2b show the highest affinity for single-stranded DNA, while BRCT binds tightest to the human G4 telomeric sequence.

Conclusion & Significance: The modular nature of these *BRCA1*-DNA interactions may provide a regulatory mechanism to control its DNA repair functions inside the cell. Therefore, we plan to perform DNA repair studies in human cell lines alongside these *in vitro* binding experiments to further test the link between DNA binding activity and repair of DNA lesions.

Biography

Ann J Fuelle is currently studying Biomedical Diagnostic and Therapeutic Sciences with concentrations in Medical Laboratory Sciences and Pre-Med studies. She started working in a laboratory at the University of Michigan in 2014 before attending Oakland University in 2016.

annfuelle@oakland.edu

Zhouling He is currently studying Biochemistry with a Biology minor. Zhouling hopes to obtain a PhD degree in the future. Both women work under the direction of Colin G. Wu at Oakland University in the field of Biochemistry studying DNA repair pathways.

zhoulinghe@oakland.edu

Notes: