Assessing the Effects of Inherited Mutations on PALB2 Structure and Function

Davis Martin
ASSESSING THE EFFECTS OF INHERITED MUTATIONS ON PALB2 STRUCTURE AND FUNCTION

By: Davis Martin

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PALB2 Repairs DNA Damage with BRCA1 and BRCA2

Radiation, chemicals, stress, etc.

DNA damage

BRCA1

BRCA2

PALB2

DNA damage

CANCER FORMATION
The Structure of PALB2

Variants of Unknown Significance (VUS)
Project Goals

1. Test a new *in vitro* method for determining the effects of VUS on PALB2 function

2. Classify VUS as detrimental or benign
The Structure of PALB2 and its Coiled-Coil Domain

N-terminal side

Coiled-Coil Domain

AA 1 | AA 14 | AA 41

C-terminal Side

WD40 Domain

AA 853 | AA 1186

PALB2

a, a'

PALB2
Identifying VUS for Testing
Goal 1: Isothermal Titration Calorimetry (ITC)

Reference cell (PALB2 buffer only)

Thermometer

Experimental cell (PALB2  )

Syringe with BRCA1 (▲)

Reference cell (PALB2 buffer only)

Thermometer

Experimental cell (PALB2  +BRCA1▲)

Syringe
ITC Can be Used to Measure Differences in Binding Affinities for PALB2 Mutants

Binding Constant of PALB2:BRCA1 (M⁻¹)

- WT PALB2
- L35P PALB2
- L24F PALB2
- K30N PALB2

No Data