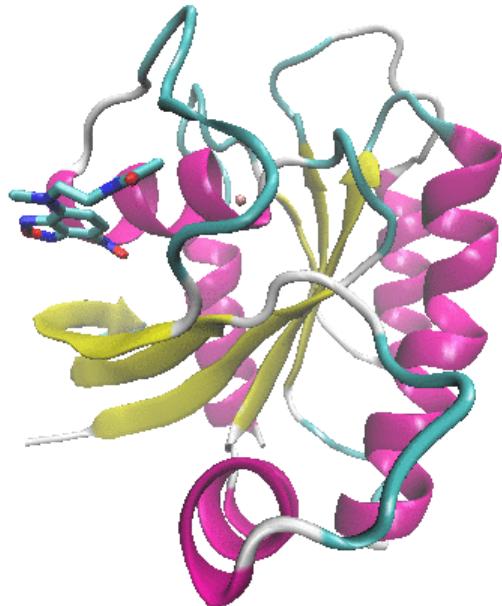


# Costello-Syndrom – A consequence of K117R variant in H-Ras

Paloma Tödtli & Bastien Canonica

8<sup>th</sup> of October 2019

# Properties of H-Ras



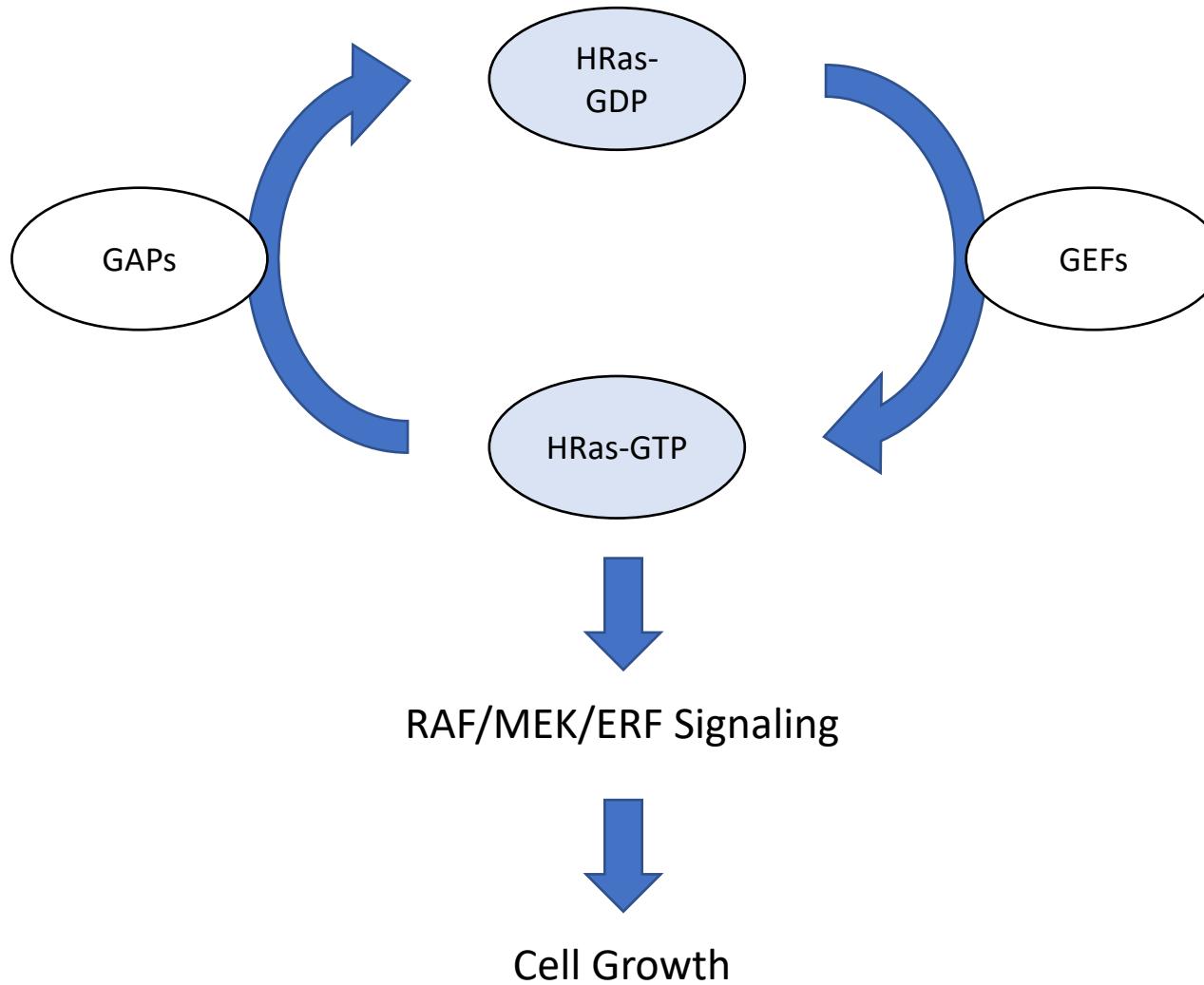
PDB ID : 2CE2

- Cellular location
  - Cell membrane
  - Golgi apparatus
- 189 amino acids
  - 5 alpha helices
  - 6 beta sheets
- Ligands
  - GDP/GTP

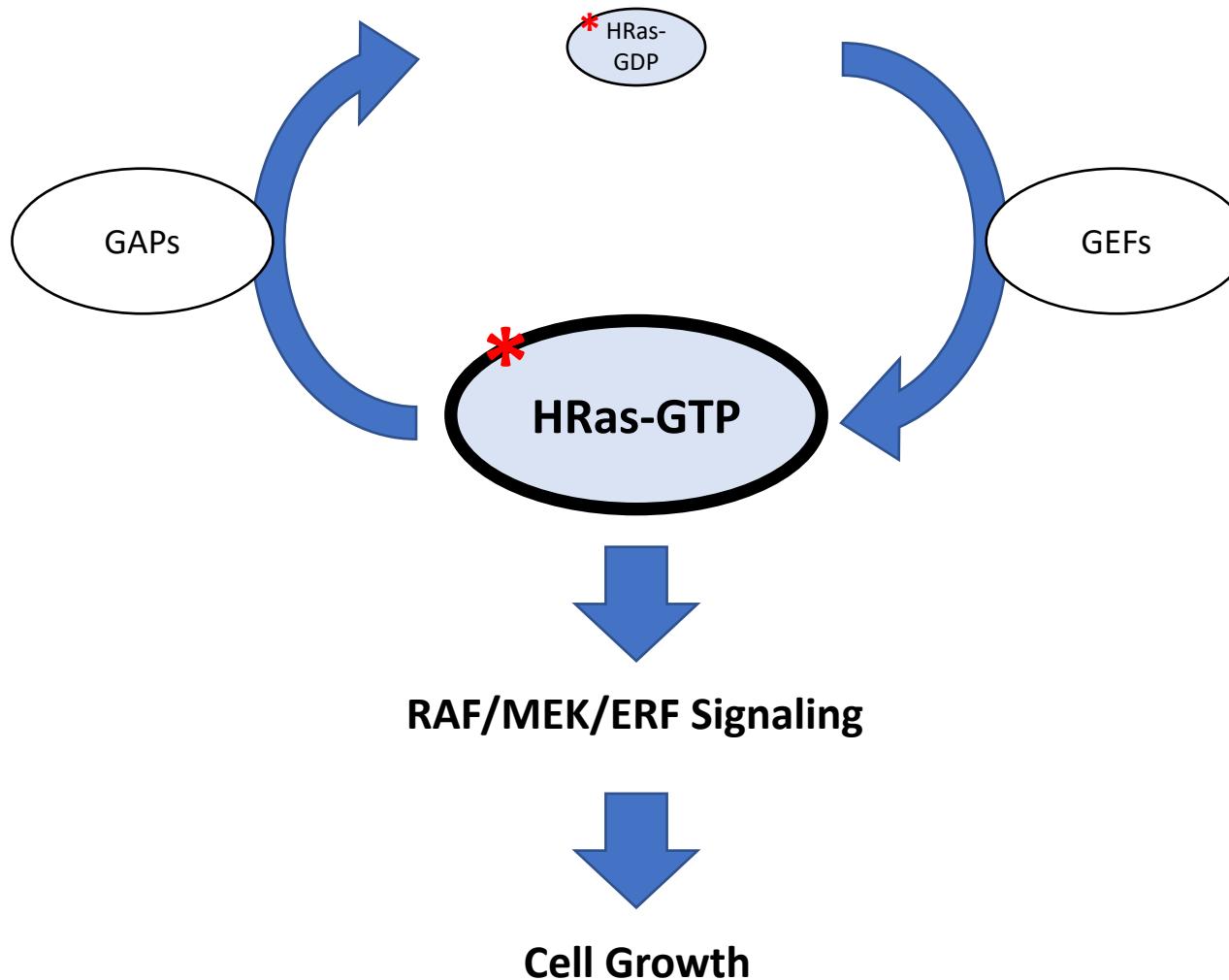
# Conservation of H-Ras

Homo_sapiens	1	MTEYKLVVV GAGGVGKSA	LTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDIL	DTAG	60
Rattus_norvegicus	1	MTEYKLVVV GAGGVGKSA	LTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDIL	DTAG	60
Mus_musculus	1	MTEYKLVVV GAGGVGKSA	LTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDIL	DTAG	60
Gallus_gallus	1	MTEYKLVVV GAGGVGKSA	LTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDIL	DTAG	60
Bos_taurus	1	MTEYKLVVV GAGGVGKSA	LTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDIL	DTAG	60
Canis_lupus	1	MTEYKLVVV GAGGVGKSA	LTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDIL	DTAG	60
Felis_catus	1	MTEYKLVVV GAGGVGKSA	LTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDIL	DTAG	60
		*****	*****	*****	
Homo_sapiens	61	QEESAMRDQYMRTGEGLCVFAINNTKSFEDIHQYREQIKRVD	KDSDDVPMVLVGNKC	DL	120
Rattus_norvegicus	61	QEESAMRDQYMRTGEGLCVFAINNTKSFEDIHQYREQIKRVD	KDSDDVPMVLVGNKC	DL	120
Mus_musculus	61	QEESAMRDQYMRTGEGLCVFAINNTKSFEDIHQYREQIKRVD	KDSDDVPMVLVGNKC	DL	120
Gallus_gallus	61	QEESAMRDQYMRTGEGLCVFAINNTKSFEDIHQYREQIKRVD	KDSDDVPMVLVGNKC	DL	120
Bos_taurus	61	QEESAMRDQYMRTGEGLCVFAINHVKSFEDIHQYREQIKRVD	KDSDDVPMVLVGNKC	DL	120
Canis_lupus	61	QEESAMRDQYMRTGEGLCVFAINNTKSFEDIHQYREQIKRVD	KDSDDVPMVLVGNKC	DL	120
Felis_catus	61	QEESAMRDQYMRTGEGLCVFAINNTKSFEDIHQYREQIKRVD	KDSDDVPMVLVGNKC	DL	120
		*****	*****	*****	
Homo_sapiens	121	AARTVESRQAQDLARSYGIPYIETSAKTRQVEDAFYTLVREIRQHKLRLNPPDESGPG			180
Rattus_norvegicus	121	AARTVESRQAQDLARSYGIPYIETSAKTRQVEDAFYTLVREIRQHKLRLNPPDESGPG			180
Mus_musculus	121	AARTVESRQAQDLARSYGIPYIETSAKTRQVEDAFYTLVREIRQHKLRLNPPDESGPG			180
Gallus_gallus	121	PARTVETRQAQDLARSYGIPYIETSAKTRQVEDAFYTLVREIRQHKLRLNPPDESGPG			180
Bos_taurus	121	AARTVESRQAQDLARSYGIPYIETSAKTRQVEDAFYTLVREIRQHKVRKLSPPDEGGPG			180
Canis_lupus	121	AARTVESRQAQDLARSYGIPYIETSAKTRQVEDAFYTLVREIRQHKVRKLSPPDEGGPG			180
Felis_catus	121	AARTVESRQAQDLARSYGIPYIETSAKTRQVEDAFYTLVREIRQHKVRKLSPPDEGGPG			180
		*****	*****	*****	
Homo_sapiens	181	CMSCKCVLS			189
Rattus_norvegicus	181	CMSCKCVLS			189
Mus_musculus	181	CMSCKCVLS			189
Gallus_gallus	181	CMNCKCVIS			189
Bos_taurus	181	CLSCRCLLS			189
Canis_lupus	181	CMSCKCLLS			189
Felis_catus	181	CMSCKCLLS			189
		*:.*:.*:*			

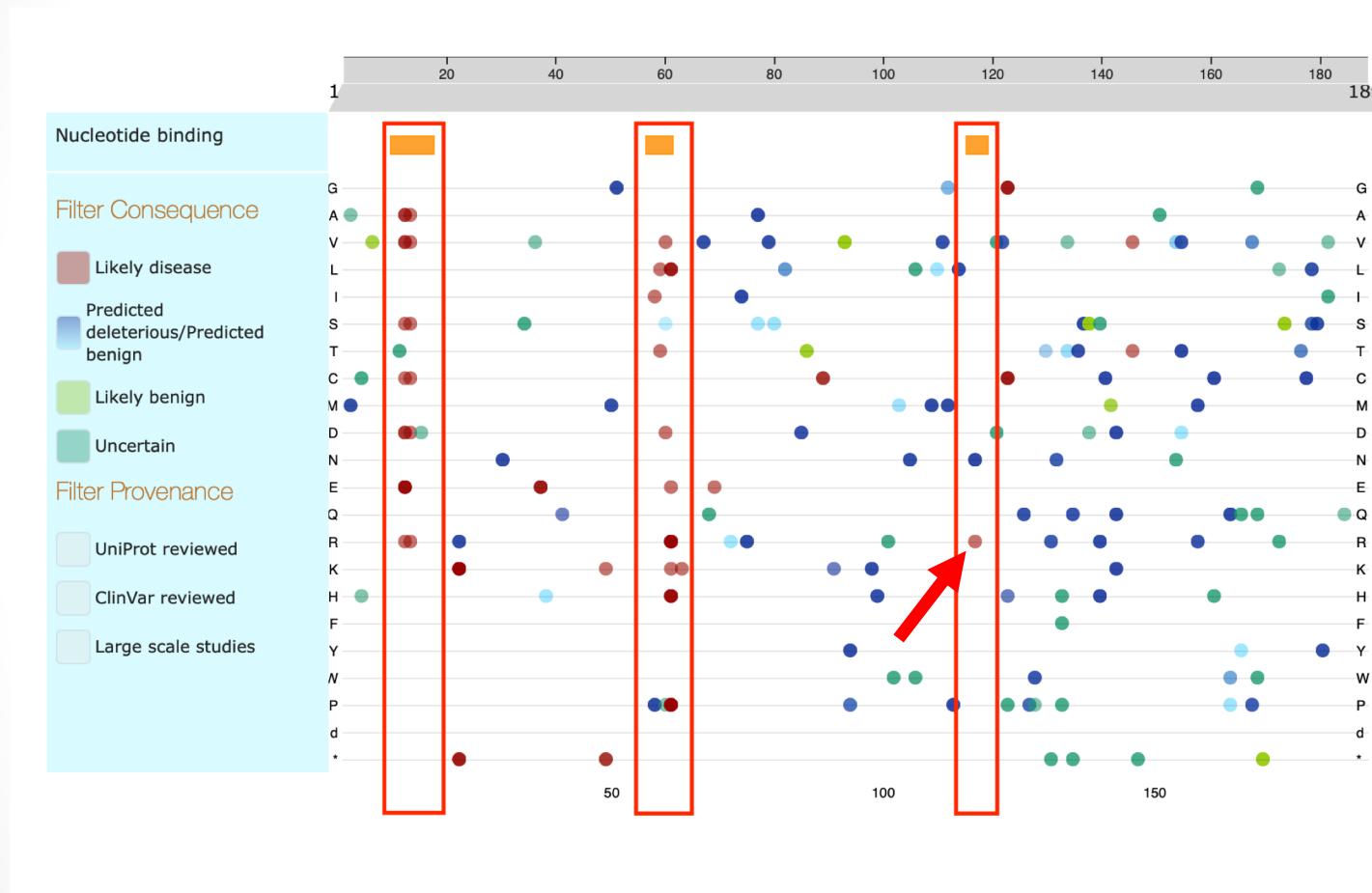
# Function of H-Ras



# Function of H-Ras



# Variants in H-Ras

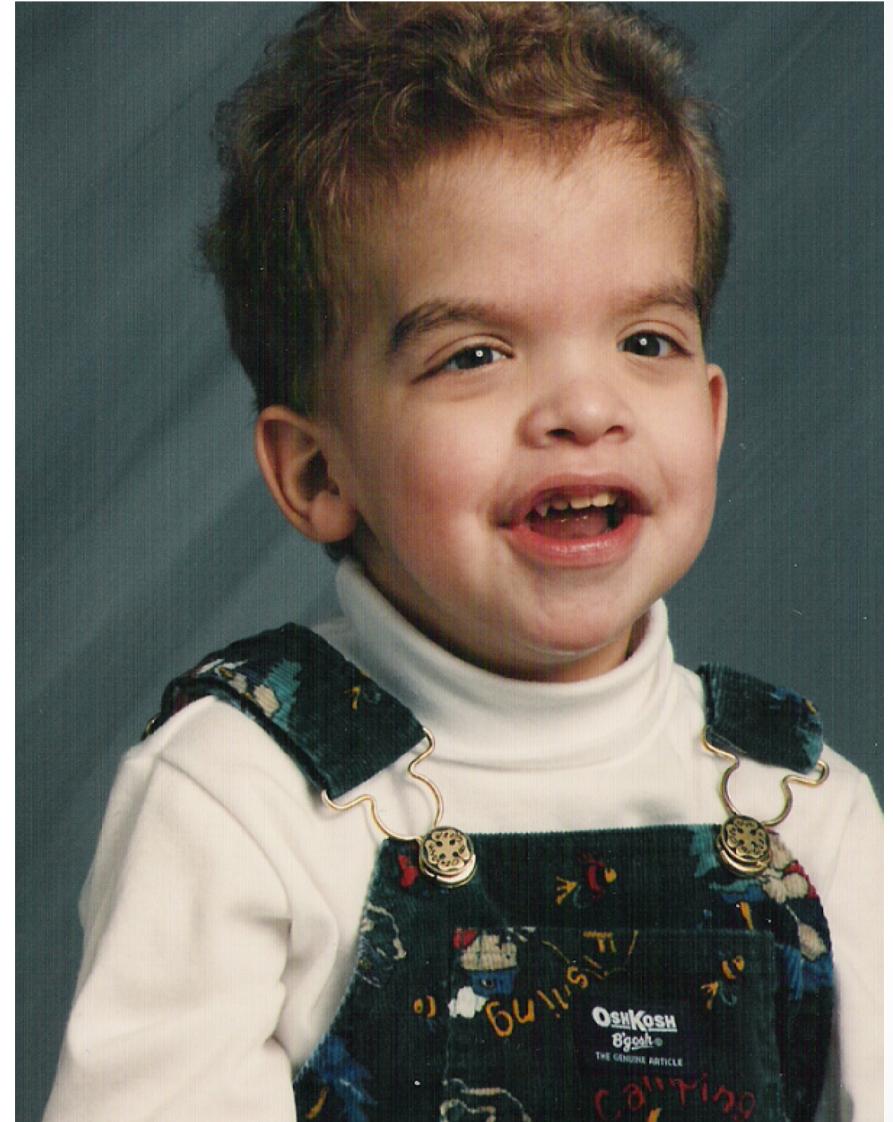


- Over 600 coding variants (EVA EMBL-EBI)
- Mutations in binding site are likely disease
- K117R :
  - PolyPhen 2 score : 1.000

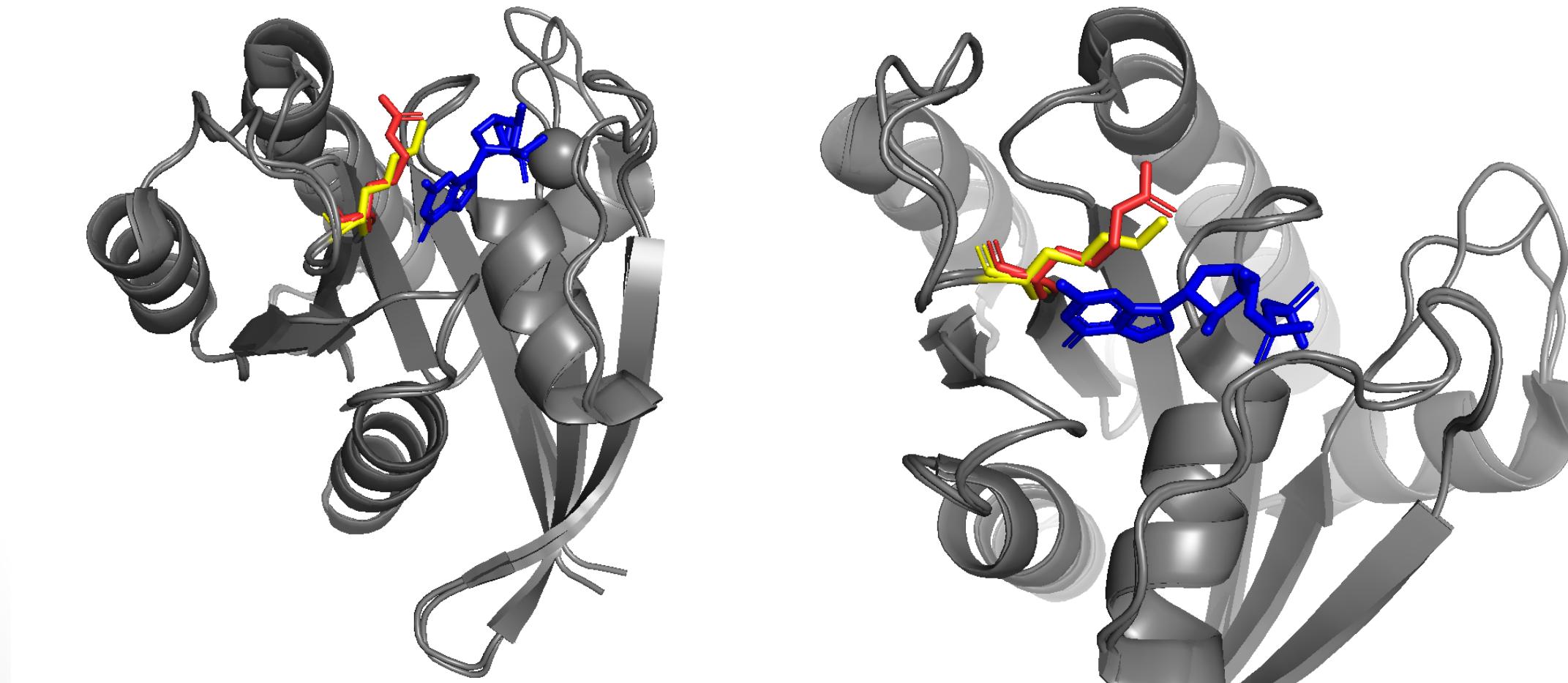
# Costello Syndrom

Not a cancer !

- Autosomal dominant
- Development and intellectual disability
- SNV in chr11 AAG > AGG
- Caused by K117R mutation



# K117R Variant



*Thank you for your attention!*

*Any question?*