

# **Targeting BTB Domain Proteins in Cancer Therapeutics**

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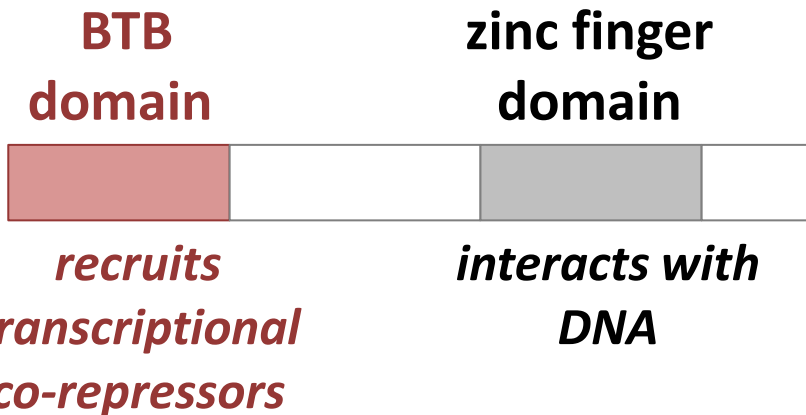
**School of Biology, FBS**

# BTB-Domain Proteins

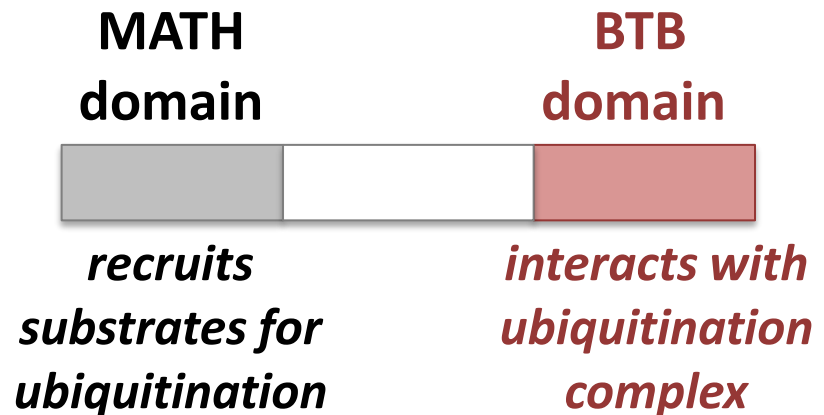
## BTB domain

- BTB: bric-a-brac, tramtrack and broad complex
- 120 residues long
- functions as a protein-protein interaction domain in eukaryotic transcription factors and in adaptor proteins of protein ubiquitination complexes

## transcription factors



## adaptor proteins



# Targeting BTB-Domain Proteins

## Biological Roles of BTB Domain Proteins

- Many BTB domain proteins play roles in development
- Several BTB domain proteins are over-expressed in specific human cancers, eg:
  - BCL6 - B-cell lymphoma
  - Nac1 - ovarian cancer
  - SPOP - kidney cancer

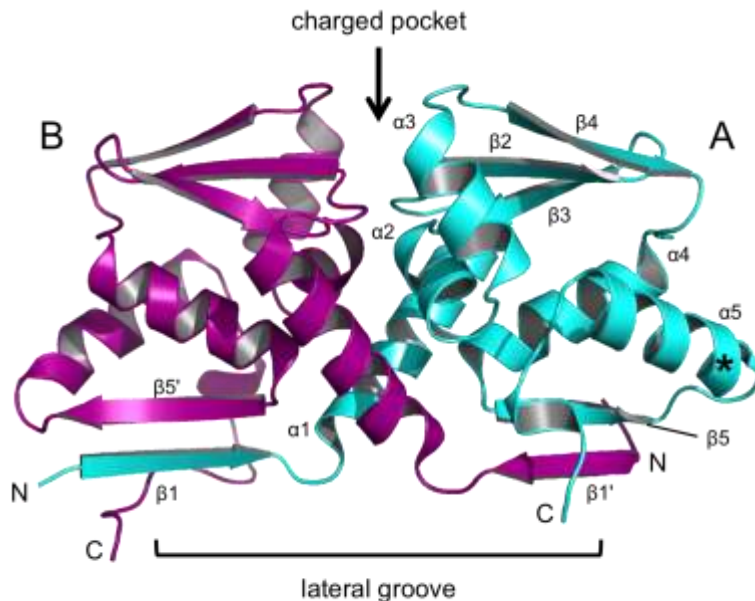
## Strategy

- Crystal structures of BTB domains
- Identify critical residues of BTB domain protein-protein interaction interfaces, eg:
  - interactions with transcriptional co-repressors
  - interactions of BTB-domain proteins with each other
  - high-order oligomerisation of BTB-domain proteins

# Targeting BTB-Domain Proteins

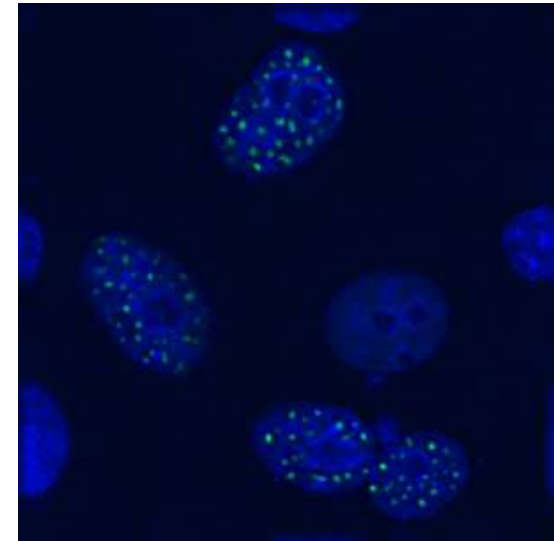
## X-ray Crystal Structures

- Miz1, BCL6, Nac1, Bach2 and SPOP BTB domains
- SPOP high-order oligomerisation



**Nac1**

cartoon representation  
of the BTB domain



**SPOP**

Functions as high-order  
oligomers in discrete nuclear  
bodies in mammalian cells

## **Current Funding**

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## **Leeds Collaborations**

**Colin Fishwick  
Simon Connell**