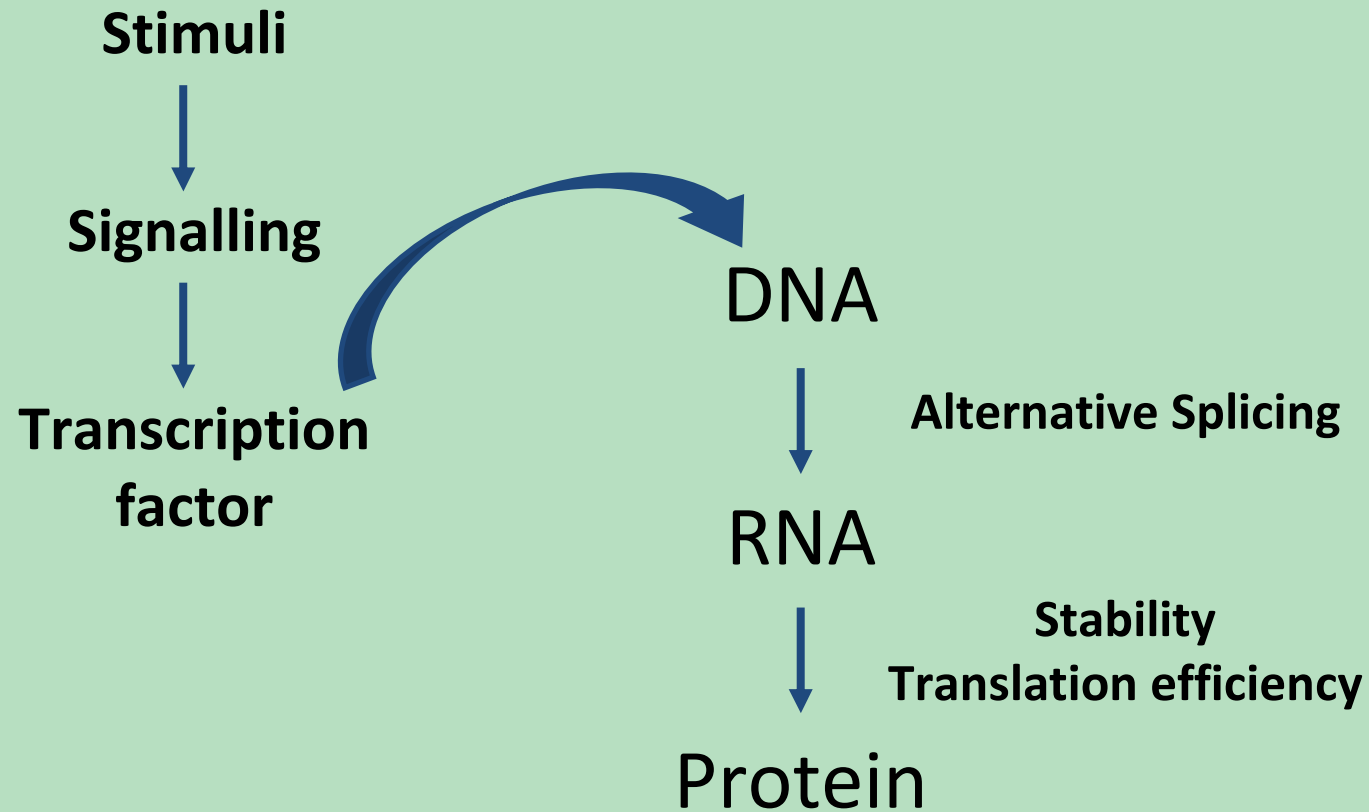


# Transcriptional regulation by antagonistic promoter binding of BCL-6 or STAT5 is modulated by Rac1 signalling

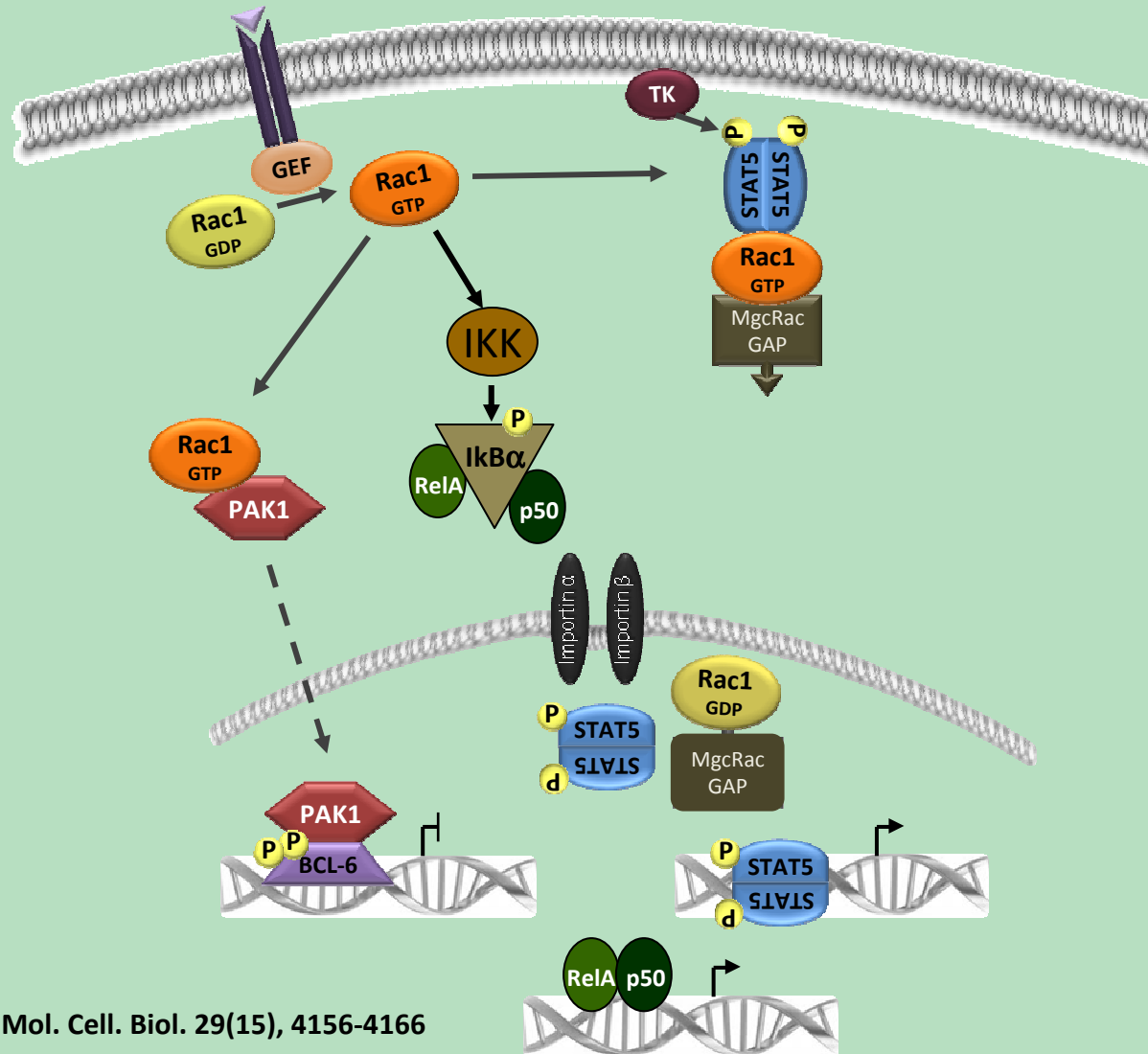
Patrícia Barros, Peter Jordan, Paulo Matos

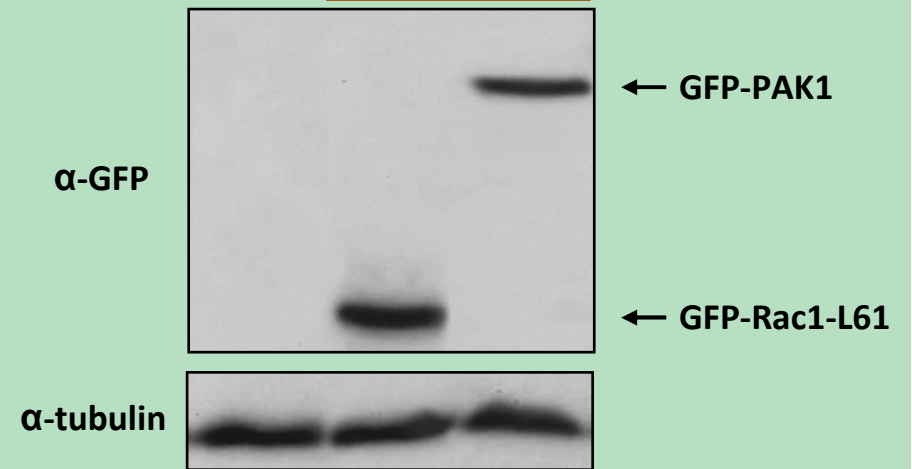
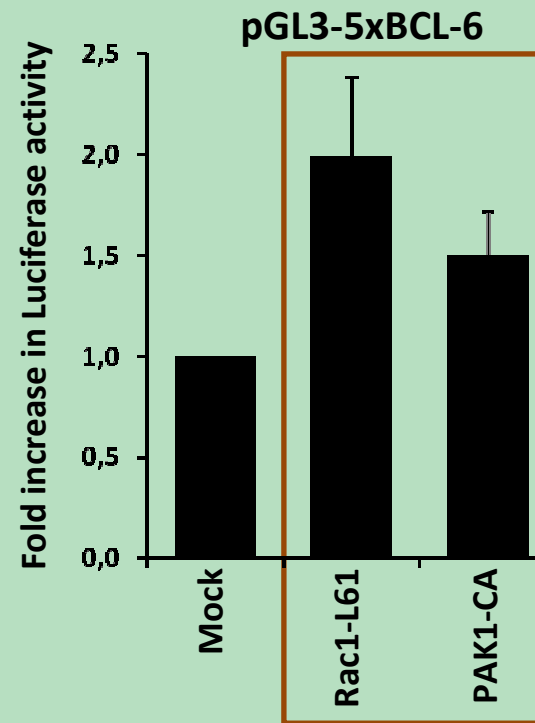
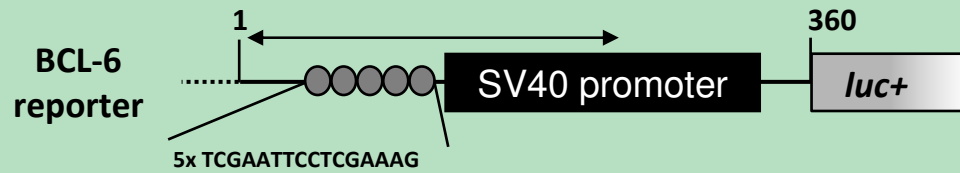
RNA 2012

# The control and flow of gene expression

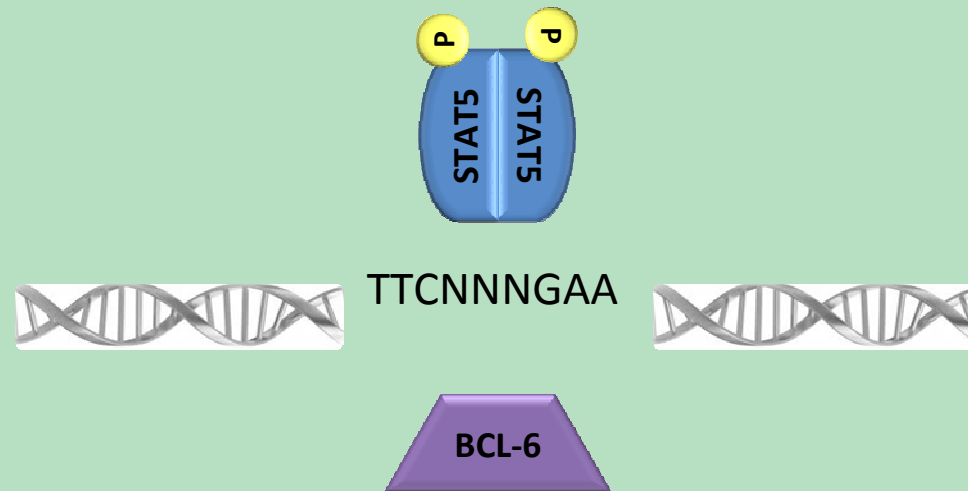


# Rac1 signalling affects transcriptional control



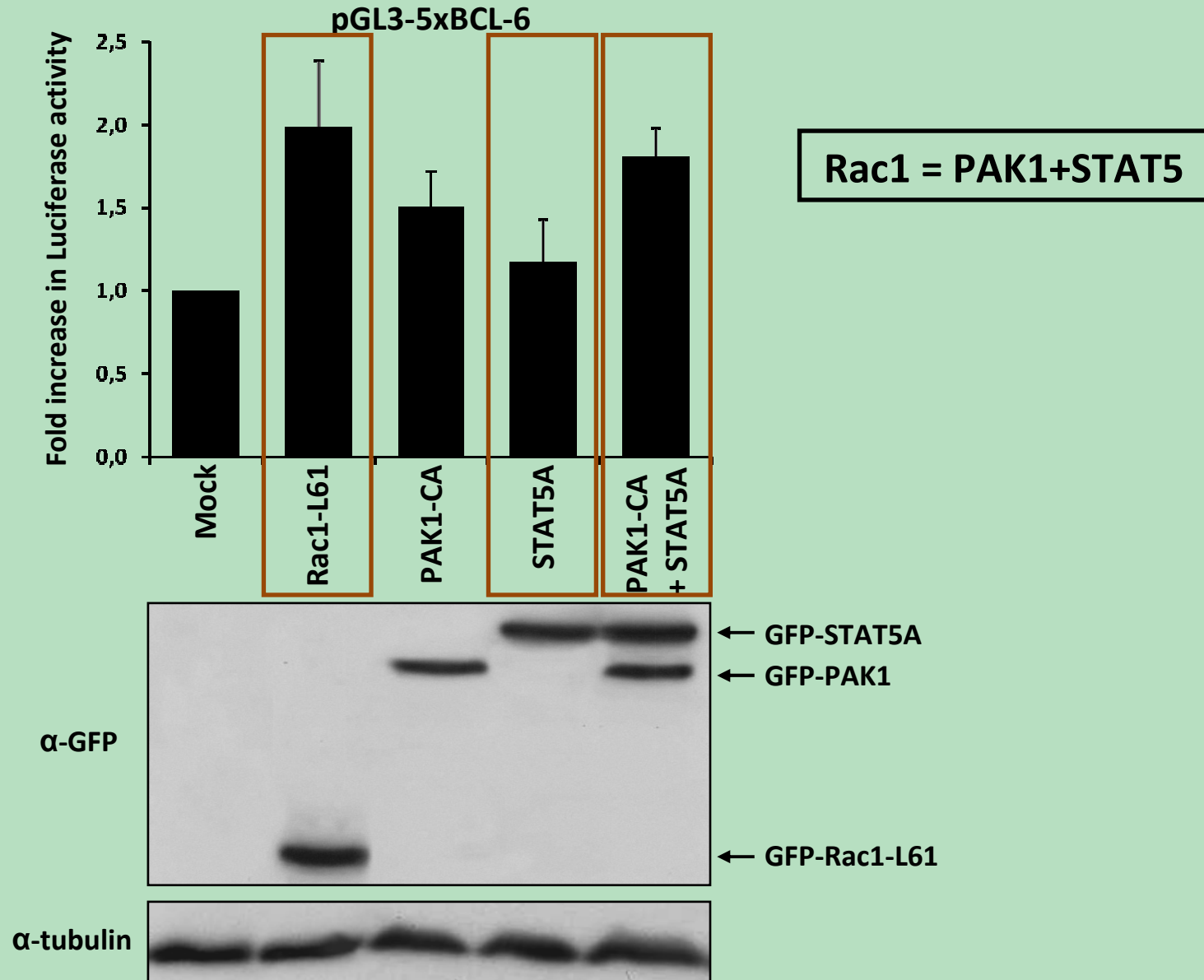


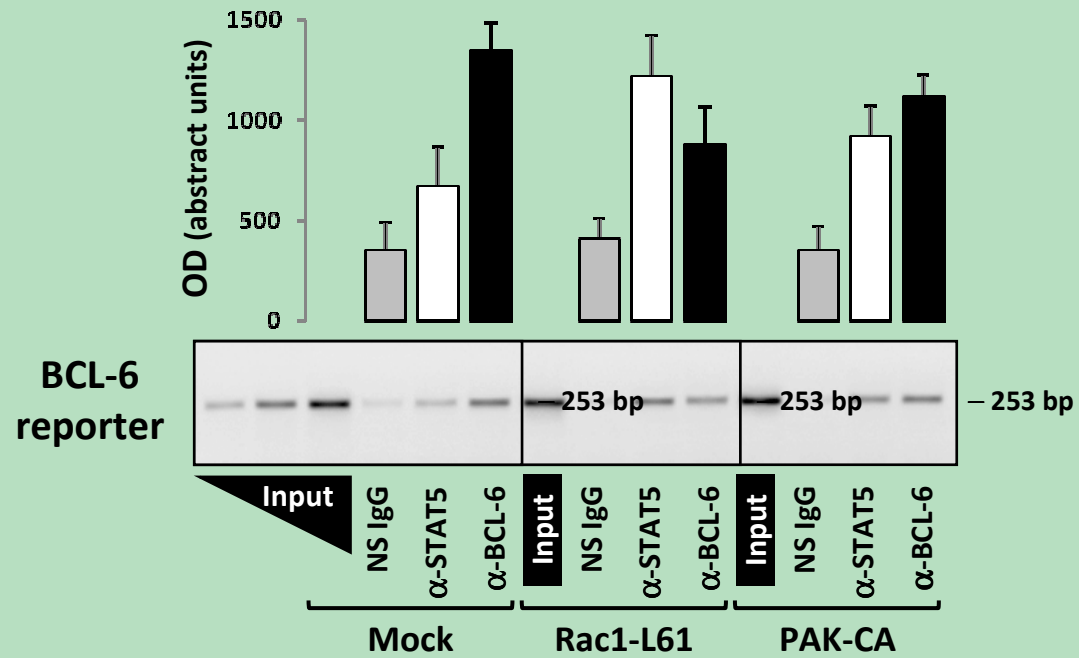
## BCL-6 and STAT5 recognise a similar core binding motif



Genes reported to be regulated by both factors:  
**cyclin D2, blimp-1, BCL-XL, Socs2, prolactin**

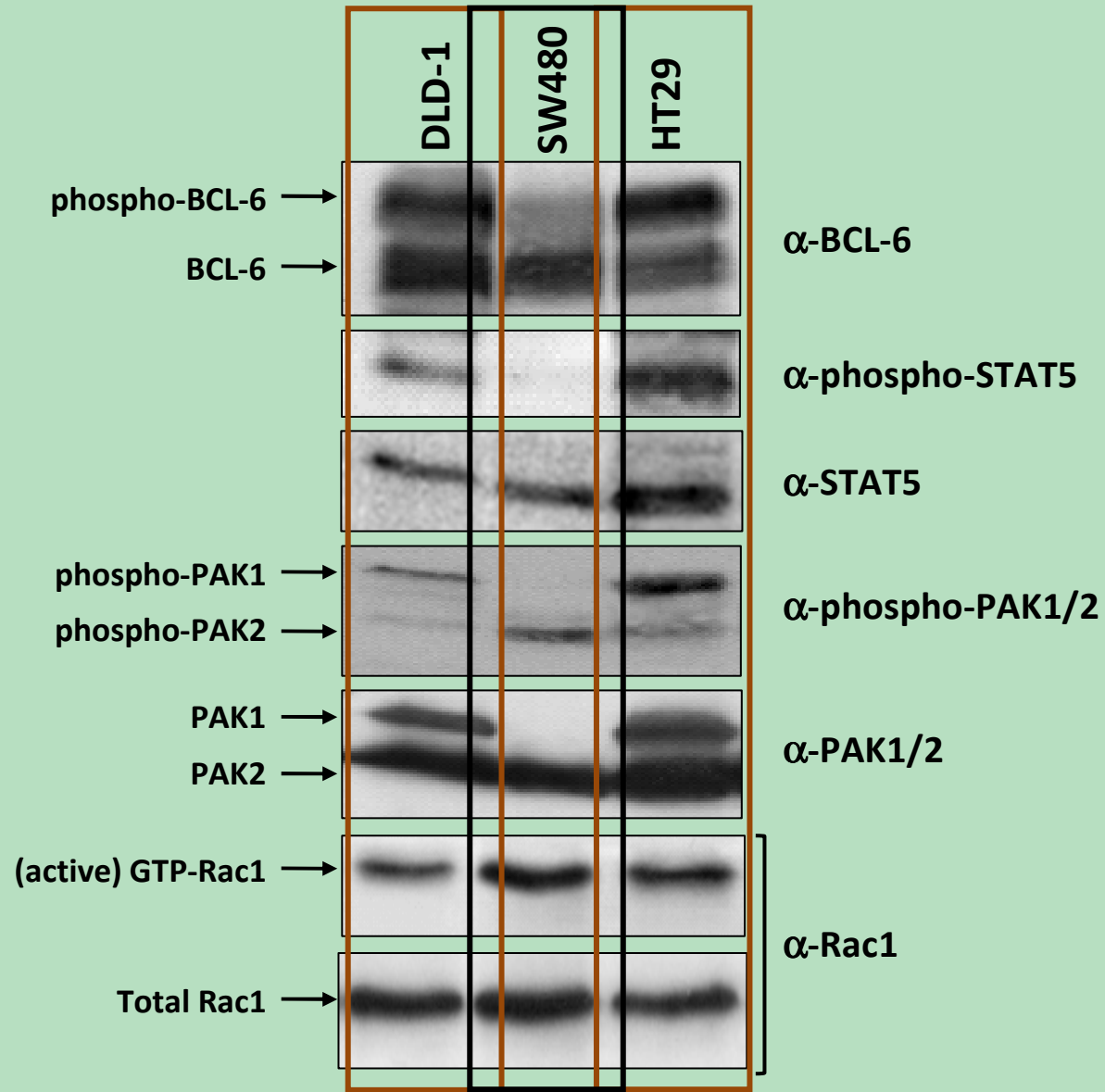
# Does Rac1 signalling coordinate the activity of BCL-6 and STAT5?





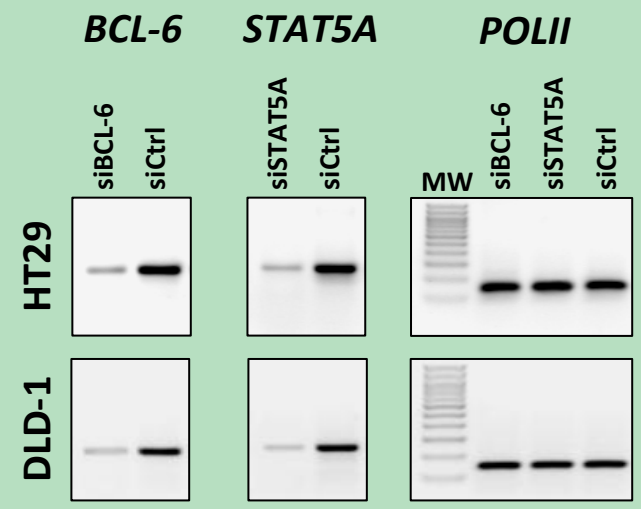
Active Rac1 promotes a switch from BCL-6 to STAT5 at the promoter.

**Does BCL-6/STAT5 transcription switching  
happens in cells?**



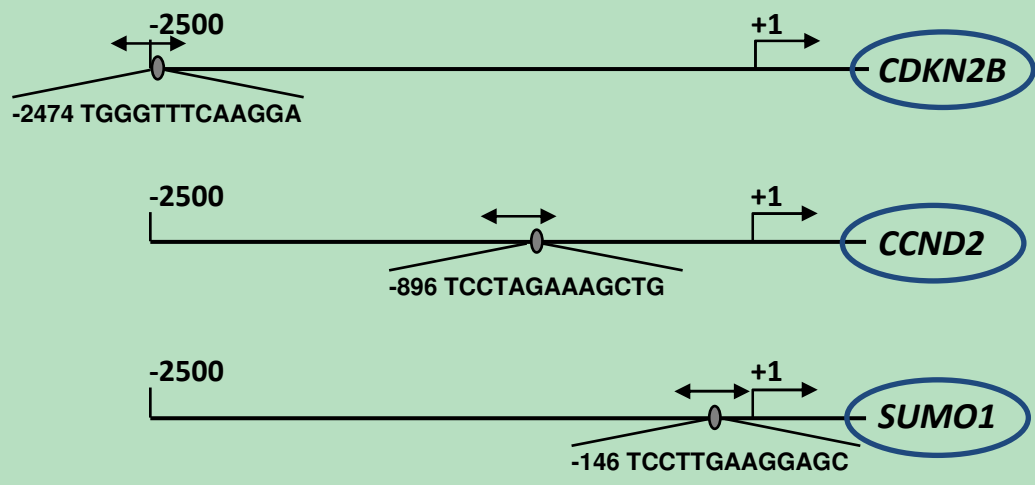
**Which endogenous genes may be targets of the transcription factor switch?**

Gene	STAT5A		RC1 6	
	DLD-1	HT29	DLD-1	HT29
ABL1				
ANAPC7				
ANAPC4				
DIRAS3				
ATM				
ATR				
BAX				

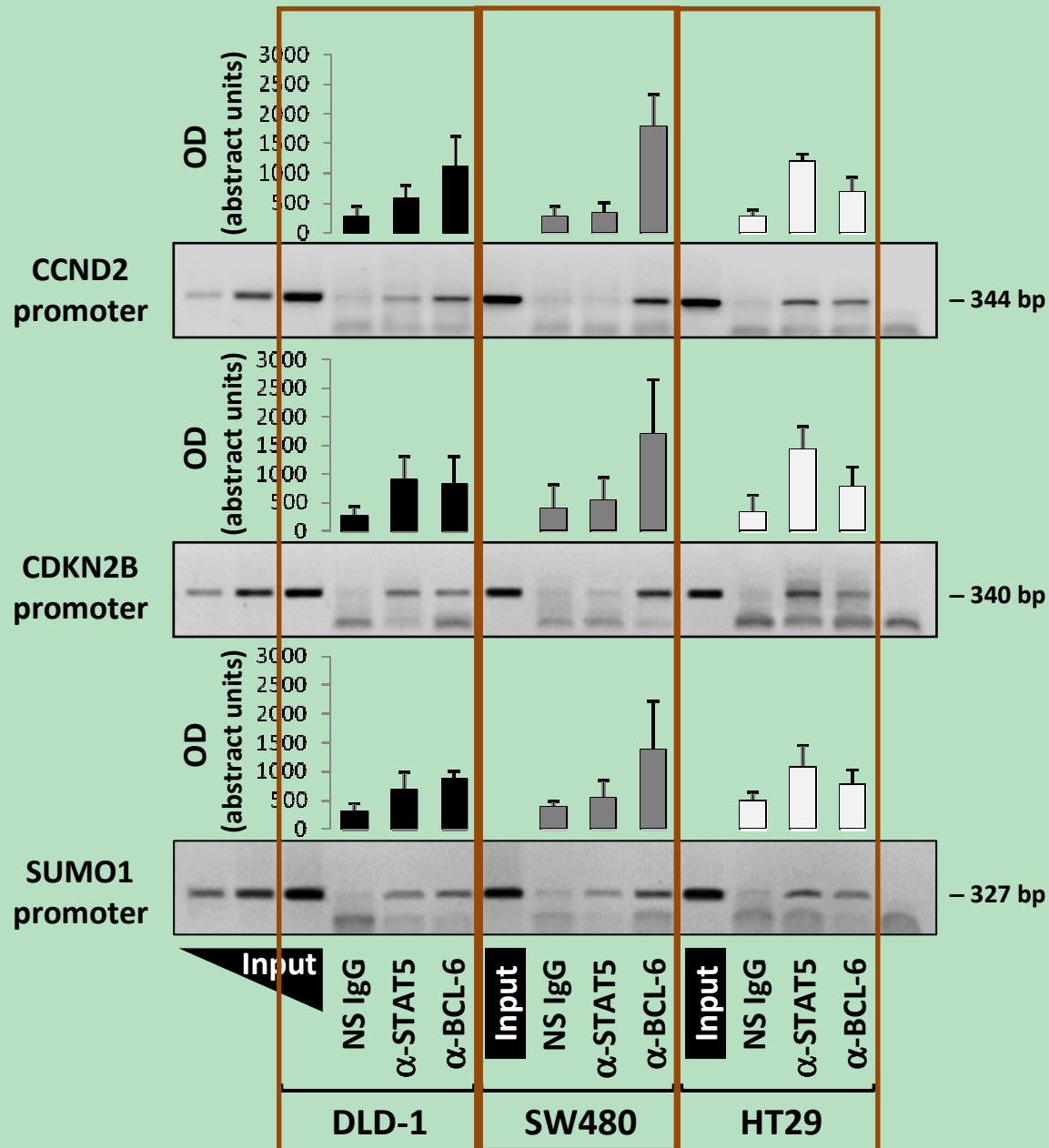


### Cell cycle PCR array

- Convert Total RNA to cDNA.
- Add cDNA to RT<sup>2</sup> qPCR Master Mix & Aliquot Mixture Across PCR Array.
- Run in Your Real-Time PCR Instrument.
- Data Analysis.



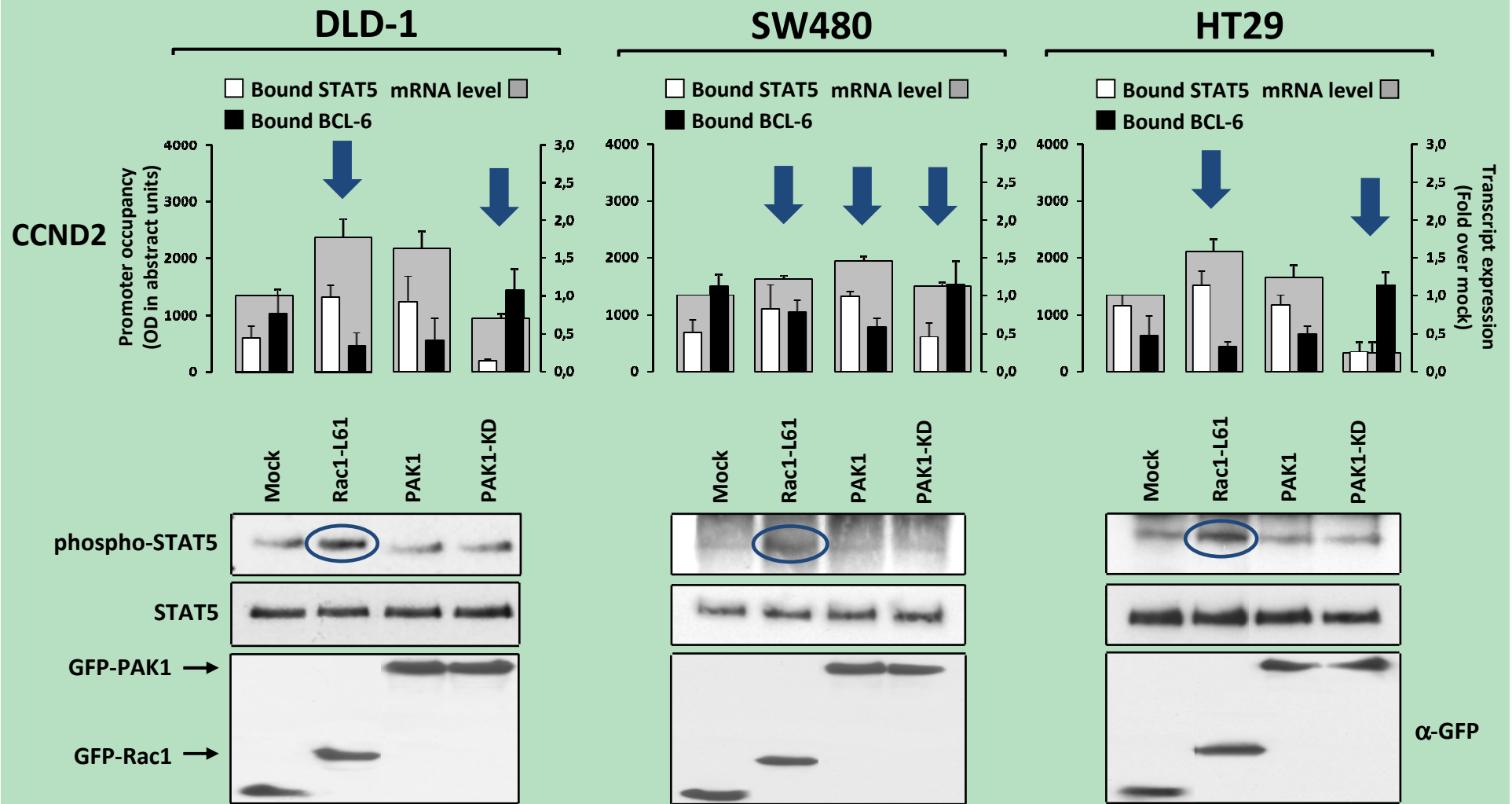
RBL2				
RPA3				
SERTAD1				
SKP2				
SUMO1				
TAF11P1				
TAF11P2				
TP53				
UBA1				



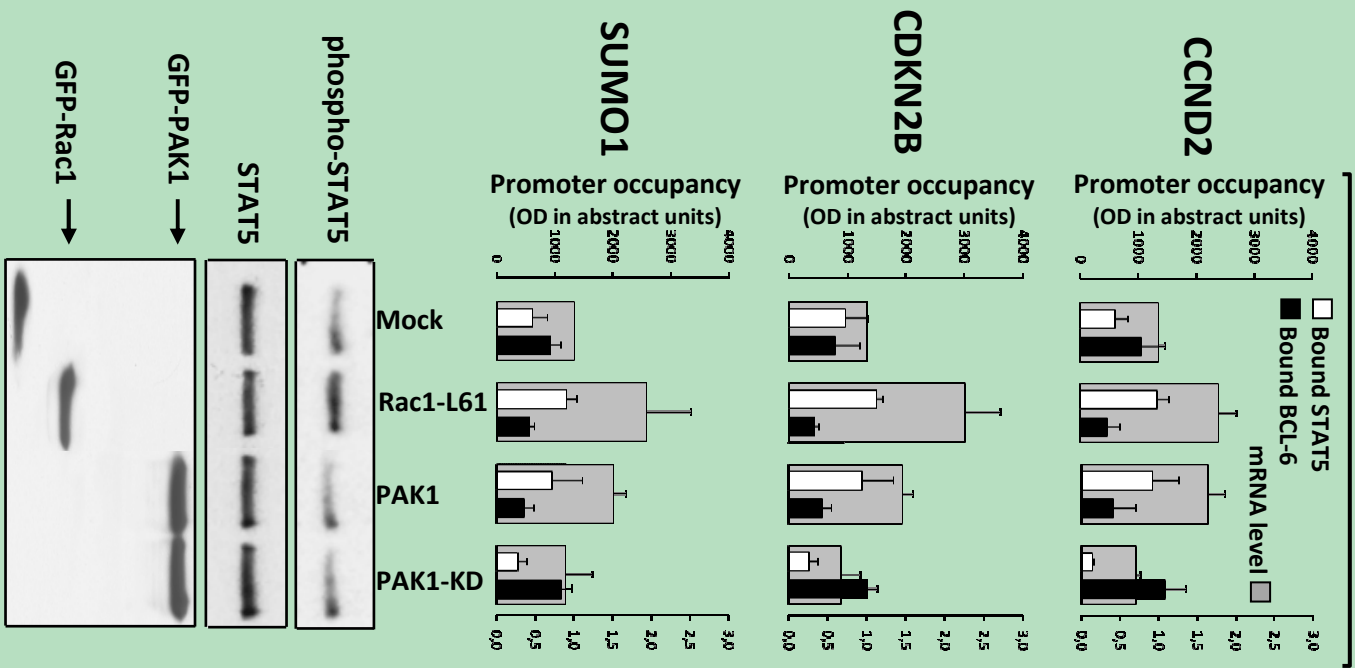
**SW480**  
 +++ Active Rac1  
 0 Active PAK1  
 + Active STAT5

**HT29**  
 + Active BCL-6  
 ++ Active Rac1  
 ++ Active PAK1  
 ++ Active STAT5

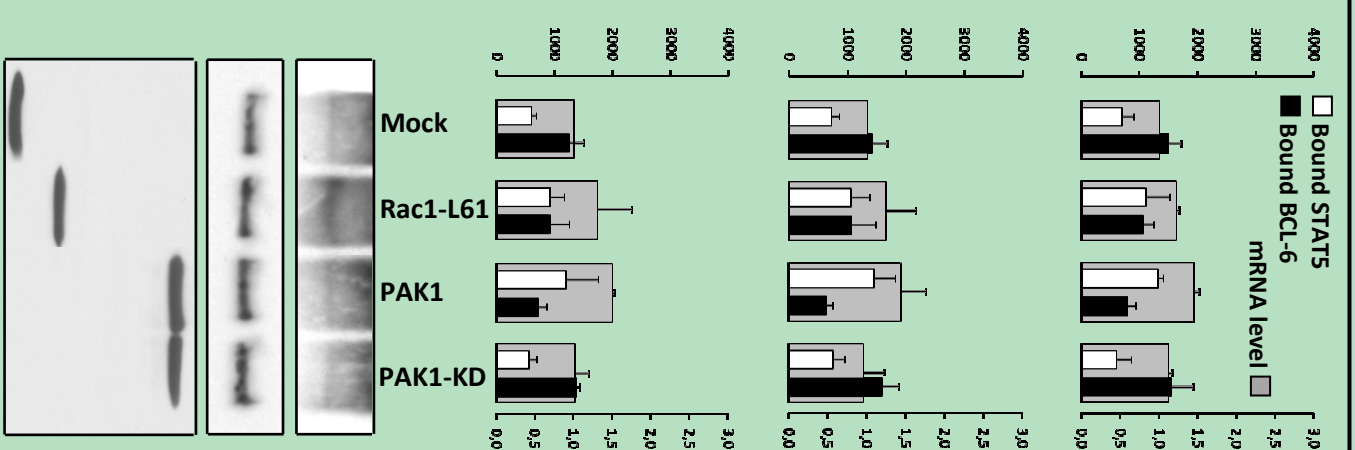
**DLD-1**  
 ++ Active BCL-6  
 + Active Rac1  
 + Active PAK1  
 + Active STAT5  
 + Active BCL-6



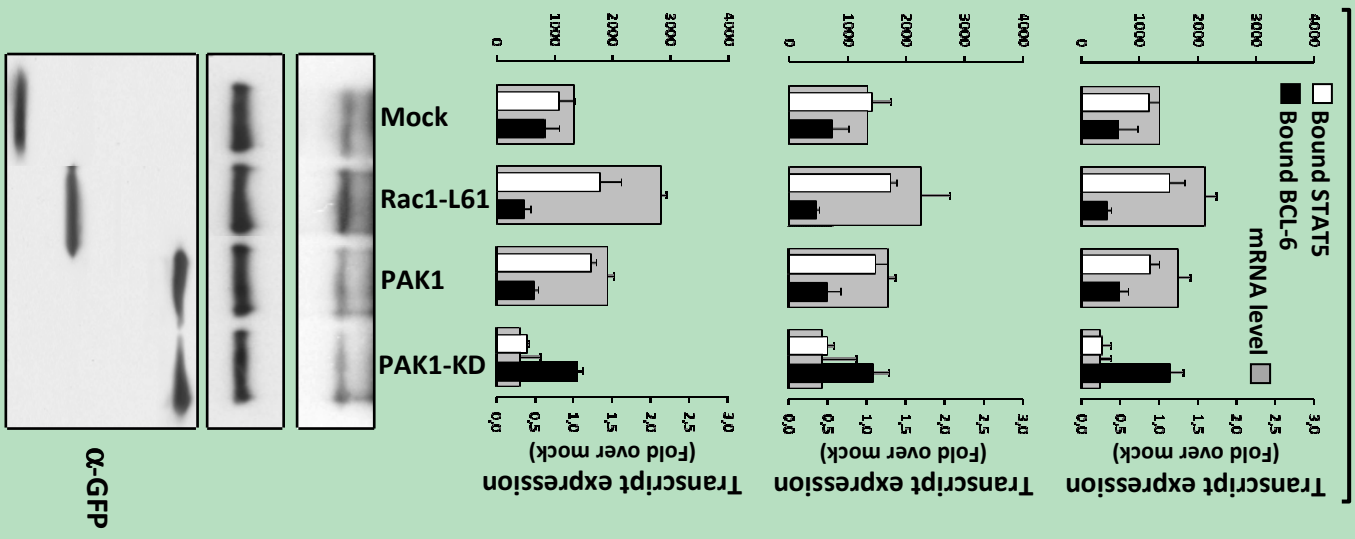
## DLD-1



## SW480



## HT29

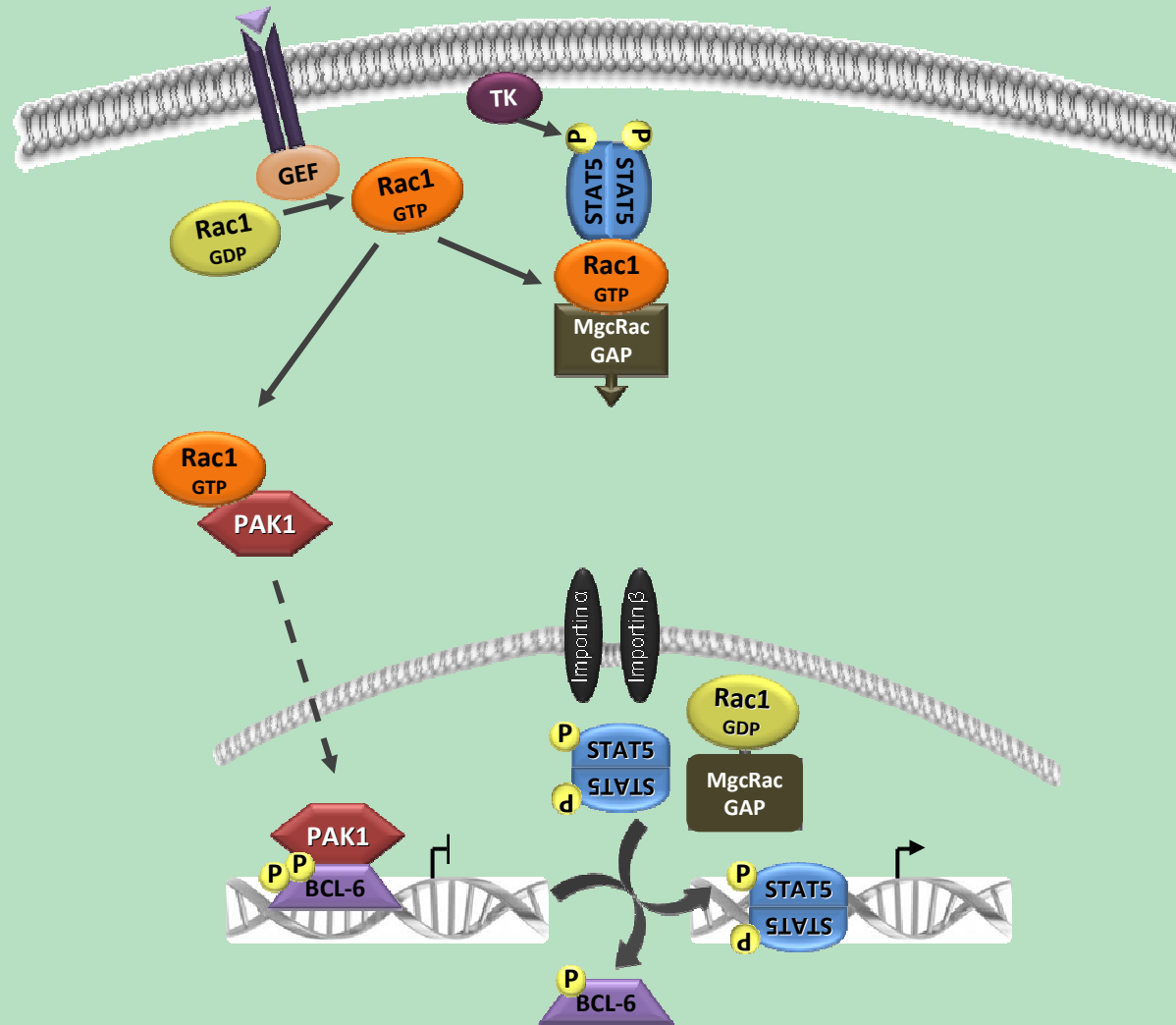


## Summary

Novel insights into the modulation of gene transcription by GTPase signalling.

- cyclin D2, CDKN2B and SUMO1 were identified to be inversely regulated by BCL-6 and STAT5 in colorectal cells.
- Rac1 signalling activates gene transcription by inducing a switch from repressor BCL-6 to activator STAT5 at their promoters.

# Proposed model



# Acknowledgements

## INSA

Paulo Matos

Peter Jordan

Sónia Moniz

Vânia Gonçalves

## Imperial College London

Eric Lam

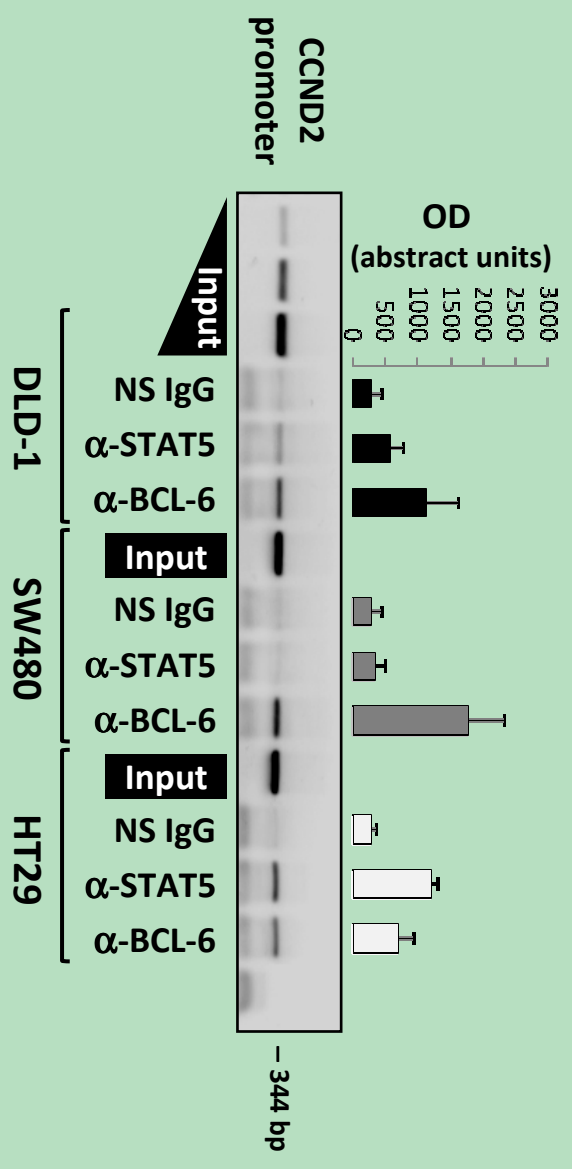
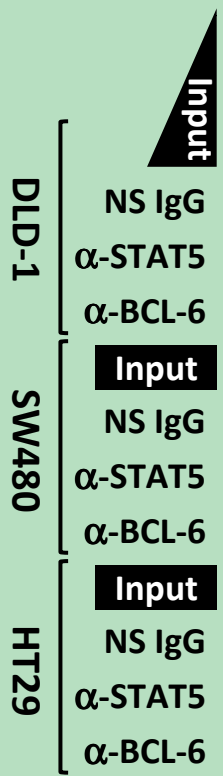
## Funding

FCT

BioFig

EMBO

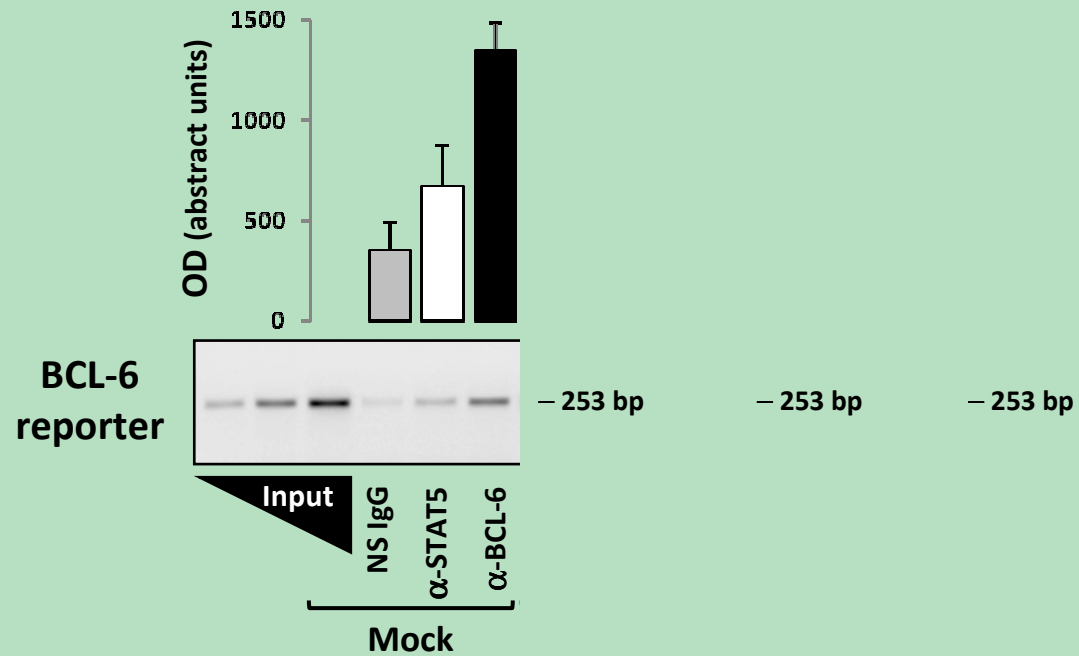




Cyclin D2: regulatory subunit of CDK4 or CDK6 required for cell cycle G1/S transition

The SUMO1 gene encodes a small ubiquitin-like protein that can be covalently attached to proteins as a monomer or a lysine-linked polymer. Unlike ubiquitin, sumoylation is not involved in proteolytic degradation of the attached protein but rather modulates nuclear transport or transcriptional regulation

CDKN2B encodes the cyclin-dependent protein kinase inhibitor protein p15 encoded by the INK4b locus, which can form a complex with CDK4 or CDK6, and prevent the activation of the kinases by cyclin D, inducing cell cycle arrest.



Active Rac1 promotes a switch from BCL-6 to STAT5 at the promoter.

# Acknowledgements

- **FCT**
- **BioFig**
- **EMBO**
- **Paulo Matos and Peter Jordan**
- **Sónia Moniz and Vânia Gonçalves**
- **Eric Lam**