- 5. Because of its ability to suppress proliferative signalling, **p16 represents important** tumour suppressor proteins.
- 6. **P21 can overcome sequestration** by cyclinD-Cdk4/6 following its elevated expression in response to the tumour suppressor p53.

## **RB** loss in Retinoblastoma and other tumours:

- 1. In addition to inhibiting E2F, RB also positively regulates differentiation-specific gene expression.
- 2. Differentiation of retinoblasts (and possibly therefore their exit from the cell cycle) may be acutely dependent on RB.
- 3. Additionally, RB loss is **not** just associated with retinoblastomas, i.e. RB1 gene deletion is also found in sarcomas, lung cancers, bladder tumours, mammary tumours and prostate cancers.
- 4. Significantly, tumours that retain normal RB often exhibit other alterations in the Rb pathway, i.e. elevated activity of the RB kinases (Cdk4,6/CyclinD).
- 5. Rb mutations are the rate limiting factors of retinoblastoma but are in no way indication that they are the **only changes needed**. tesale.co.uk

## P53:

- Dy the TP53 gene. 1. p53 is a 53Kda transcription factor en
- 2. p53 monomers associate to man 177 Kda tetrainer, which is recruited to p53specific response tements in the promoter of erget genes.
- 3. WT p 3 to how vely suppress of O coe-mediated cellular transformation.
- p53 is a key node in signaling networks involved in sensing cellular stress, in that, it 4. integrated different cell signals to produce appropriate responses that will benefit the organism.

