**A**

"Constitutive" model

- p53
- Developmentally essential genes
- Normal development

- p53 loss
- Developmentally essential genes (partially loss)
- Functional redundant players (e.g. p63, p73)
- Low penetrance of developmental defect at the population level

**B**

"Passive" model

- p53
- No stress
- No activation
- Apoptosis, cell cycle arrest and differentiation
- The levels of developmentally essential genes are normal
- Normal development

- Stress
- Activation
- Apoptosis, cell cycle arrest and differentiation
- Dys-regulation of developmentally essential genes (stochastic)
- Normal development at the population level

- p53 loss
- Stress
- No activation
- Apoptosis, cell cycle arrest and differentiation
- Dys-regulation of developmentally essential genes (stochastic)
- Low penetrance of abnormal development at the population level