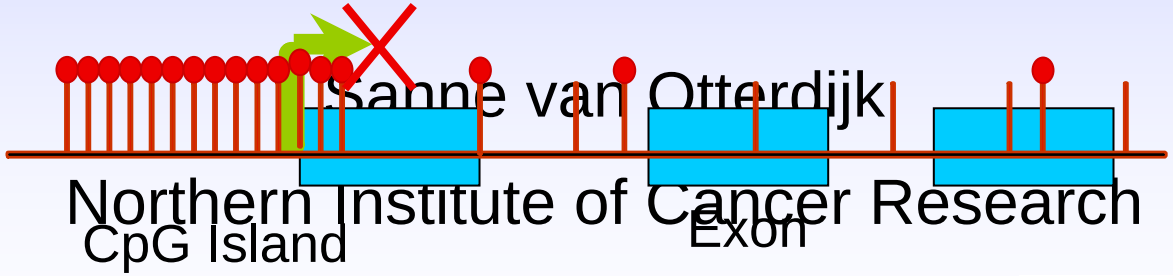
Does childhood leukaemia develop in cells which are pre-primed by the presence of aberrant patterns of DNA methylation?



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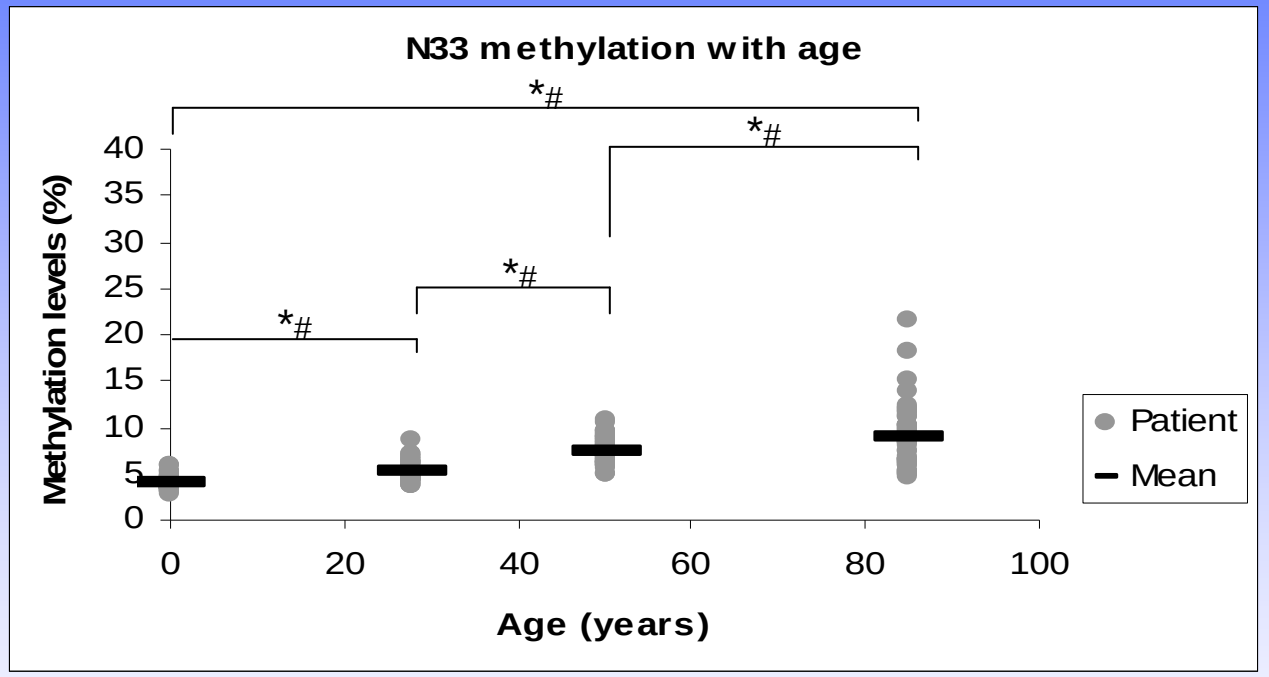
Aims

- Understand how abnormal methylation develops in and contributes to haematological malignancies
  - Quantify the extent and variability of DNA methylation in healthy populations at different ages
  - Quantify the extent and variability of DNA methylation in childhood and adult ALL patients at different stages of the disease
  - Examine the overlap between methylation patterns in healthy individuals and ALL patients
  - Assess the potential of differential methylation in apparently healthy samples for leukaemia risk assessment or detection of early disease
  - Assess the potential of differential methylation in ALL remission samples for prediction of outcome

DNA methylation is increasing with age

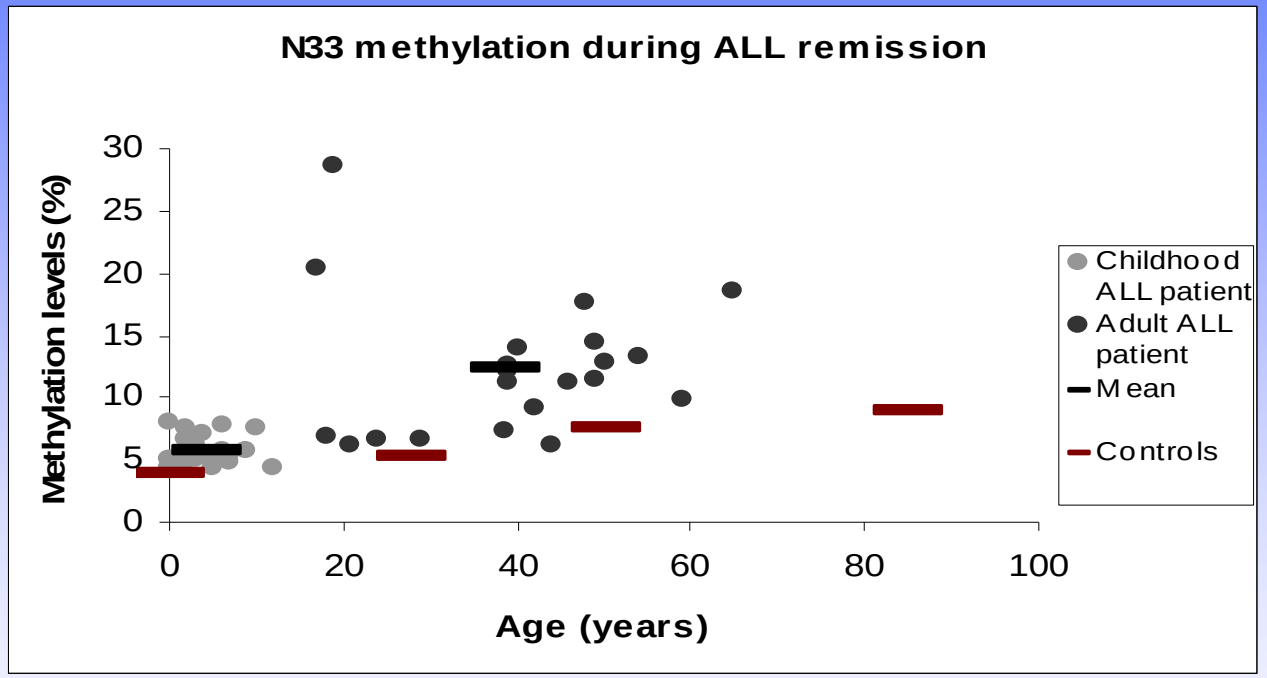


* A significant difference in methylation levels is observed

A significant difference in variance of methylation is observed

Similar patterns observed in 4 other leukaemia related genes;
TWIST2, HOXD4, EphA10 and *HAND2*

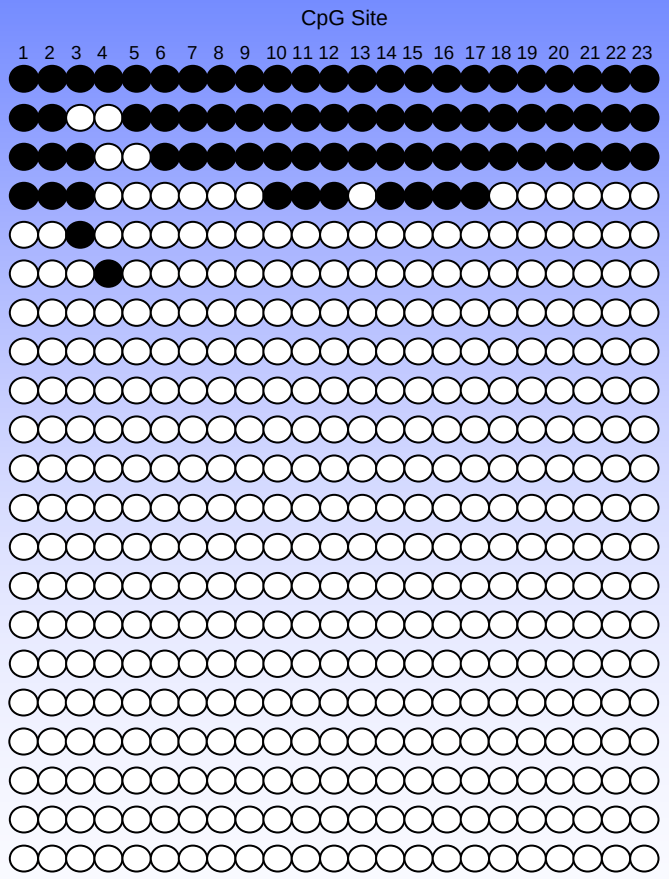
DNA methylation during ALL remission



Similar patterns observed in 4 other leukaemia related genes;
TWIST2, HOXD4, EphA10 and *HAND2*

“Leukaemia-like” features are already present in healthy individuals

TWIST2

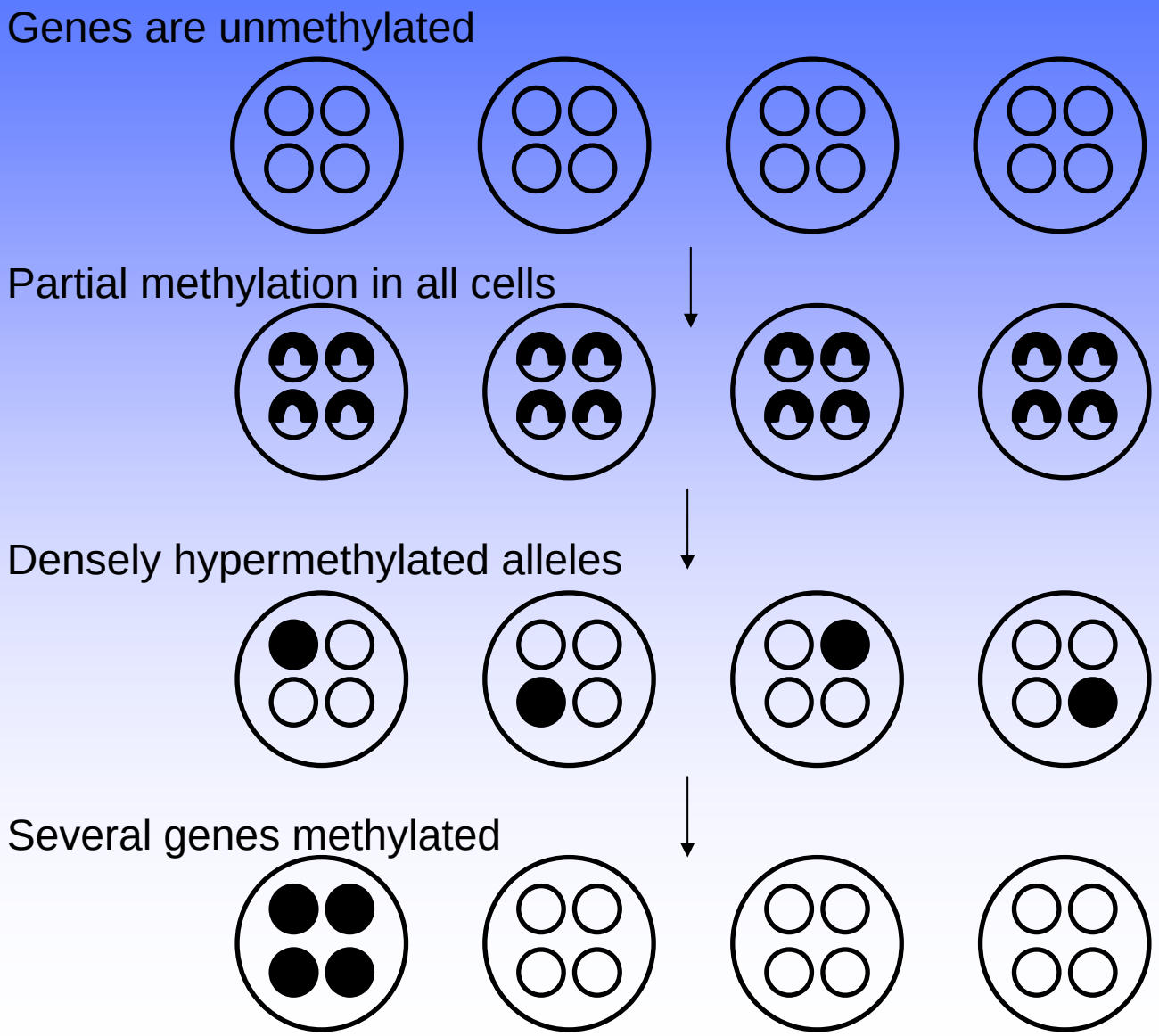


Gene	*TWIST2*	*HOXD4*	*EphA10*	*N33*
TWIST2				
HOXD4	**R Value = 0.51** **p value = 0.0002**			
EphA10	**R value = 0.55** **p value = 0.00004**	**R value = 0.36** **p value = 0.01**		
N33	**R value = 0.49** **p value = 0.0003**	**R value = 0.72** **p value = 5.0E-09**	**R value = 0.31** **p value = 0.03**	
HAND2	**R value = 0.43** **P value = 0.001**	**R value = 0.64** **p value = 7.0E-07**	**R value = 0.38** **p value = 0.006**	**R value = 0.64** **p value = 0.000002**

Highly methylated alleles

CIMP

Pre-existing methylation may underlie susceptibility to cancer



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