

ICR

The Institute
of Cancer Research

**GWAS identifies three loci, implicating the
planar cell polarity pathway and the
MYCN-DDX1 2p24.3 amplicon region in
Wilms tumor susceptibility**

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Childhood Cancer 2012**

Wilms tumor

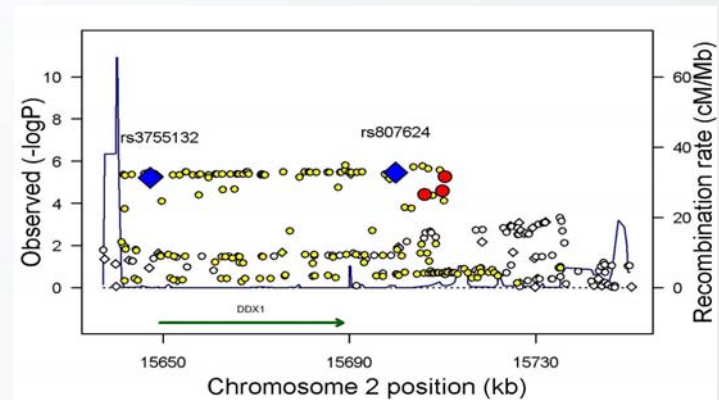
- Childhood kidney tumor that affects 1 in 10,000 children
- Median age of diagnosis is 3 – 4 years
- Evidence for a genetic basis for Wilms
 - Incidence rates in migrant populations match that of their parent population rather than their host population
 - 2% of cases have a family history of Wilms
 - Several known genetic causes of Wilms – *WT1* & *11p15*
- Underlying cause unknown in 95% unselected cases

GWAS

- GWAS is used to identify common, low risk genetic variants that cause disease
- Scanned ~600,000 common variants distributed across the whole genome
- Compared variant genotypes between cases and controls
- Variants showing significant differences were verified in a second series of cases and controls
- 4 variants within 3 regions were found to be more common in Wilms tumor patients than controls

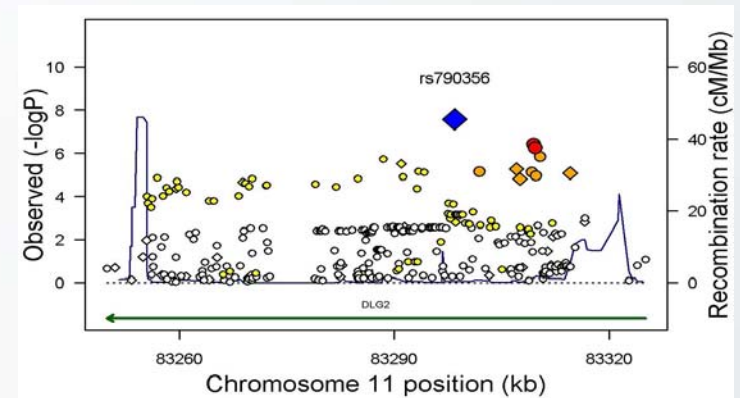
rs3755132 & rs807624 – *DDX1*

- $P = 1.03 \times 10^{-14}$ and 1.32×10^{-14}
- 109 kB linkage region on 2p24.3
- Both variants associate with the region independently
- MYCN is 250 kB from *DDX1* and both genes are often amplified in childhood tumors



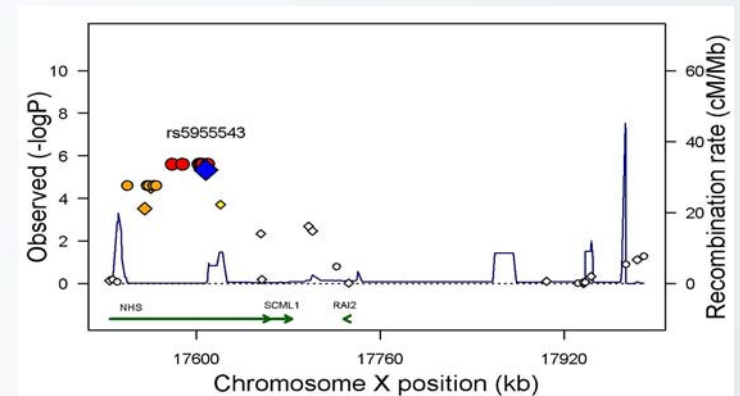
rs790356 – *DLG2*

- $P = 4.35 \times 10^{-15}$
- 68 kB linkage region on 11q14.1
- *Drosophila* homolog, *dlg*, interacts with Scribble and Lgl
- Scribble and Lgl are both Planar Cell Polarity Pathway genes
- *SCRIB* expression is activated by WT1



rs5955543 – *NHS*, *SCML1* & *RAI2*

- $P=1.04 \times 10^{-9}$
- 403 kB linkage region on Xp22.13
- *NHS* homologous to *gukh*, which in *Drosophila* facilitates interaction between Dlg and Scribble
- *SCML1* and *RAI2* control developmental processes and cell fate determination



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The Wilms Tumor
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