<table>
<thead>
<tr>
<th>Title</th>
<th>Role of RET and PHOX2B gene polymorphisms in risk of Hirschsprung’s disease in Chinese population [9]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author(s)</td>
<td>Miao, X; GarciaBarceló, MM; So, MT; Leon, TYY; Lau, DKC; Liu, TT; Chan, EKW; Lan, LCL; Wong, KKY; Lui, VCH; Tam, PKH</td>
</tr>
<tr>
<td>Citation</td>
<td>Gut, 2007, v. 56 n. 5, p. 736</td>
</tr>
<tr>
<td>Issued Date</td>
<td>2007</td>
</tr>
<tr>
<td>URL</td>
<td><a href="http://hdl.handle.net/10722/57411">http://hdl.handle.net/10722/57411</a></td>
</tr>
<tr>
<td>Rights</td>
<td>This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.; Gut. Copyright © B M J Publishing Group.</td>
</tr>
</tbody>
</table>
Role of RET and ko=PHOX2B gene polymorphisms in risk of Hirschsprung’s disease in Chinese population


Gut 2007;56:736
doi:10.1136/gut.2006.116145

Updated information and services can be found at:
http://gut.bmj.com/cgi/content/full/56/5/736

References
This article cites 10 articles, 5 of which can be accessed free at:
http://gut.bmj.com/cgi/content/full/56/5/736#BIBL

1 online articles that cite this article can be accessed at:
http://gut.bmj.com/cgi/content/full/56/5/736#otherarticles

Email alerting service
Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article

Notes

To order reprints of this article go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to Gut go to:
http://journals.bmj.com/subscriptions/
Hirschsprung's disease (OMIM 142623) is a complex congenital disorder characterised by the absence of ganglion cells of the plexus myentericus and plexus submucosus in the area of the aganglionic segment. The disease results in failure to pass meconium, chronic severe constipation, and colonic distention during the neonatal period. Since the discovery of the RET gene for Hirschsprung's disease in homozygous genotypes combined (Table 1), SNPs were in almost complete linkage disequilibrium in our population (D = 0.986, p < 0.001), only the former was selected for further analysis. Among subjects carrying at least one RET 5G allele or at least one PHOX2B G allele, the OR for Hirschsprung's disease was 1.56 (95% CI 1.09 to 2.20) or 2.98 (95% CI 1.64 to 5.44). The OR increased, however, to 11.72 (95% CI 6.35 to 21.55) among subjects carrying both the RET 5AA and PHOX2B AA genotypes (p < 0.001, test for homogeneity). The OR value of 11.72 is larger than the values of the RET 5AA and the PHOX2B AA genotypes independently (7.78±1.75 – 8.53), which indicates a more than additive interaction between the RET and the PHOX2B SNPs on risk of developing Hirschsprung's disease according to the statistical model.

To our knowledge, this is the first study to demonstrate that the interaction between RET and PHOX2B polymorphisms has a substantial impact on risk of Hirschsprung's disease. This recognised multifactorial genetic disorder requires the interaction of several unrelated genes to produce the phenotype. Both RET and PHOX2B have important roles in the development of the enteric nervous system and PHOX2B is involved in the transcriptional regulation of RET in cell lines originated from neural crest. It is therefore biologically plausible that a joint effect of RET and PHOX2B SNPs affects the risk of Hirschsprung's disease. However, the essential mechanisms behind our finding need to be investigated.

**Table 1: Risk of Hirschsprung's disease associated with RET genotypes combined with PHOX2B genotypes**

<table>
<thead>
<tr>
<th>Retotype</th>
<th>Patients (n = 256)</th>
<th>Controls (n = 242)</th>
<th>OR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GG + GA</td>
<td>19 (7.4)</td>
<td>65 (26.9)</td>
<td>1.00</td>
</tr>
<tr>
<td>GG + GA</td>
<td>57 (22.2)</td>
<td>122 (50.4)</td>
<td>1.57 (1.92–2.75)</td>
</tr>
<tr>
<td>AA + GA</td>
<td>36 (14.1)</td>
<td>15 (6.2)</td>
<td>7.96 (4.14–17.60)</td>
</tr>
<tr>
<td>AA + AA</td>
<td>144 (56.3)</td>
<td>40 (16.5)</td>
<td>11.72 (6.35–21.55)</td>
</tr>
</tbody>
</table>

*ORs and 95% CIs were calculated by unconditional logistic regression adjusting for gender.

We extend our gratitude to all subjects who participated in the study. This work was supported by the University of Hong Kong, Pok Fu Lam, Hong Kong SAR, China. The homeobox gene PHOX2B is essential for the development of autonomic neural crest derivatives. Nature 2003;119:366–70.

**References**


The incidence and risks of liver biopsy in non-cirrhotic patients: An evaluation of 3806 biopsies

Liver biopsy plays a crucial role in the diagnosis and management of liver diseases. For the past decade, this invasive procedure has become a safe one with the prevailing application of an ultrasound-guided method, the use of thinner gauge needles and improved operational techniques. Over the past years, the debatable issue of liver biopsy has mainly focused on the safety and suitability of a shorter observation time with respect to cost savings. Referring to this issue, Beddy et al even shortened their observation time to 1 hour and indicated that only one haemorrhagic complication occurred within one hour amongst 500 liver biopsy occasions. There were no recorded delayed complications or deaths at follow up. Generally, we agree with the conclusion that outpatient liver biopsy is safe when done in a...