GENETICS

Common ground

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10.1038/nrc2195

URLs

OCT4

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=gene&Cmd=ShowDetailView&TermToSearch=54606&ordinalpos=2&itool=EntrezSystem2.PEntrez.Gene.Gene_ResultsPanel.Gene_RVDocSum

POU5F1P1

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=gene&Cmd=ShowDetailView&TermToSearch=54606&ordinalpos=16&itool=EntrezSystem2.PEntrez.Gene.Gene_ResultsPanel.Gene_RVDocSum

MYC

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=gene&Cmd=ShowDetailView&TermToSearch=46096&ordinalpos=16&itool=EntrezSystem2.PEntrez.Gene.Gene_ResultsPanel.Gene_RVDocSum

Prostate cancer

<http://www.cancer.gov/cancertopics/types/prostate>

Colorectal cancer

<http://www.cancer.gov/cancertopics/types/colon-and-rectal>

Breast cancer

<http://www.cancer.gov/cancertopics/types/breast>

Earlier this year several papers identified a number of single nucleotide polymorphisms (SNPs) that were associated with an increased risk of developing **prostate cancer**. Further investigation has now shown that one of these SNPs also increases the risk of developing **colorectal cancer**, potentially indicating a common biological mechanism.

Christopher Haiman and colleagues had noted that band q24 on chromosome 8, where several prostate cancer predisposition SNPs reside, is also amplified in patients with colorectal cancer. The significance of this was unclear. These SNPs might be unrelated to colorectal cancer; they might all increase the risk of colorectal cancer (as well as prostate cancer), or the SNPs at this locus might contribute differently to the risk of developing either prostate or colorectal cancer. To address this, these authors genotyped six of the seven previously characterized prostate cancer SNPs in patients with colorectal cancer and a control population, and found that only one, rs6983267, was associated with an increased risk of developing colorectal cancer in various ethnic groups. This indicates that the other SNPs at 8q24 contribute different risks depending on tissue type. Additional analyses in this region identified two further SNPs — rs10808556 and rs7013278 — that confer significant additional risk for colorectal cancer.

The colorectal cancer SNPs identified in this study reside in a region that contains one of the **OCT4** pseudogenes, **POU5F1P1**. OCT4 is a key regulator of stem cell pluripotency and is overexpressed in some tumours, as are its pseudogenes. Moreover, the proto-oncogene **MYC** also resides close to this region, indicating that changes at 8q24 might have an effect on its expression.

DIGITALSTOCK

However, Brent Zanke and colleagues found no statistically significant association in the expression levels of **MYC** and genotype at 8q24 in patients with colorectal cancer. Using a genome-wide association study, these authors had also identified rs6983267 and another SNP, rs10505477, as markers of significant risk of developing colorectal cancer. Both SNPs effectively tag one another as they are in a recombination poor region spanning 17kb. Indeed, only two common haplotypes exist in this interval, which contain two putative open reading frames: DQ515897, which has multiple alternatively spliced products, and DQ486513, which is currently categorized as the **POU5F1P1** pseudogene.

Ian Tomlinson and colleagues were also unable to make a clear association between risk of colorectal cancer and the expression of **MYC**. This group identified rs6983267 and rs10505477 as significantly affecting the risk of developing colorectal cancer, and they showed that rs6983267 correlates with an increased risk of developing adenomas, so genetic variation at this locus might be involved in tumour

initiation. Their investigation into the expression of **POU5F1P1**, using reverse transcriptase PCR, failed to establish any obvious correlation with genotype, despite the transcript being expressed in some colorectal cancer samples, and they report that DQ515897 is not expressed in colorectal cancer samples.

All three studies show that genetic variation at 8q24 marked by rs6983267 leads to increased risk for both colorectal and prostate cancer. Interestingly, genetic variation at 8q24 was also flagged as a risk factor for **breast cancer**. Further studies are clearly required to determine how sequence variation at this locus contributes biologically to tumour development.

Nicola McCarthy

ORIGINAL RESEARCH PAPERS Haiman, C. A. *et al.* A common genetic risk factor for colorectal and prostate cancer. *Nature Genetics* 8 July 2007 (doi: 10.1038/ng2098) | Zanke, B. W. *et al.* Genome-wide association scan identifies a colorectal cancer susceptibility locus on chromosome 8q24. *Nature Genetics* 8 July 2007 (doi: 10.1038/ng2089) | Tomlinson, I. *et al.* A genome-wide association scan of tag SNPs identifies a susceptibility variant for colorectal cancer at 8q24.21. *Nature Genetics* 8 July 2007 (doi: 10.1038/ng2085)