

### This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
<b>Cancer</b>				
Colorectal cancer	$\beta$ -Catenin; jagged 1 ( <b>JAG1</b> ); notch homolog 1 translocation- associated ( <i>Drosophila</i> ) (NOTCH1); NOTCH2	<p>A study in mice and in patient samples suggests that inhibiting JAG1-mediated NOTCH activation may be useful for treating colorectal cancer. In a mouse model of <math>\beta</math>-catenin-induced colorectal cancer, deletion of one <i>JAG1</i> allele significantly decreased tumor size and growth rates compared with what was seen in controls expressing two functional copies of the gene (<math>p=0.002</math> for size and <math>p&lt;0.001</math> for growth rate). In patient-isolated colorectal adenomas, <i>JAG1</i> mRNA levels were significantly higher than those in normal intestinal tissue (<math>p&lt;0.05</math>). High levels of <i>JAG1</i> protein were localized to tumor areas containing nuclear <math>\beta</math>-catenin and were associated with increased NOTCH1 and NOTCH2 activation. Next steps include evaluating the therapeutic potential of combining NOTCH and <math>\beta</math>-catenin inhibitors in models of colorectal cancer and identifying peptides or antibodies that block the NOTCH-JAG1 interaction.</p> <p>Avalon Pharmaceuticals Inc.'s AVN316, a small molecule compound that lowers <math>\beta</math>-catenin protein levels, is in preclinical testing to treat cancer. At least five companies have compounds in development targeting the NOTCH signaling pathway, including <math>\gamma</math>-secretase inhibitors.</p> <p><b>SciBX 2(13); doi:10.1038/scibx.2009.529</b> Published online April 2, 2009</p>	Work unpatented; available for licensing from the Municipal Institute of Medical Investigation	Rodilla, V. <i>et al. Proc. Natl. Acad. Sci. USA</i> ; published online March 23, 2009; doi:10.1073/pnas.0813221106 <b>Contact:</b> Anna Bigas, IMIM-Hospital del Mar, Barcelona, Spain e-mail: <a href="mailto:abigas@imim.es">abigas@imim.es</a>