A Milestone in Cancer Genetics: deCODE Discovers First Common Genetic Variants Affecting the Risk of Many Types of Cancer

Findings point to common mechanisms of susceptibility to cancers of the lung, bladder, prostate, cervix and skin; findings to be integrated into deCODEme™, the new deCODEme Cancer Scan™, and deCODE's DNA-based risk diagnostic tests

Reykjavik, ICELAND, January 18, 2009 – Scientists at deCODE genetics (Nasdaq: DCGN) and colleagues from the US and ten European countries today announced a long-awaited first in cancer research: the discovery of common single-letter variations in the human genome (SNPs) linked to susceptibility not of one, but several different types of cancer, including those of lung, bladder, prostate, skin and cervix.

Over the past two years, deCODE has led a wave of discoveries by scientists around the world of common SNPs conferring risk of many major types of cancer. Yet without exception, these SNPs have been linked to cancer of only one or at most two tissue types or organs. The SNPs published today, located near each other on chromosome 5p15, may therefore help to tag major biological mechanisms underlying cancer suseptibility more generally. The paper, entitled "Sequence variants at the TERT-CLPTM1L locus associate with many cancer types," is published today in the online edition of *Nature Genetics* at www.nature.com/ng, and will appear in an upcoming print edition of the journal.

"Today's findings demonstrate the power of using genetics to advance our understanding of the biology of cancer and to discover new strategies for assessing and reducing risk. Our next task is to discover how these SNPs affect susceptibility. One plausible, but as yet unproven, explanation is that these variants provide a genetic background that determines how our bodies respond to environmental risk factors. A thread connecting these different cancer types is that most have important known environmental risk factors and all tend to arise in the tissue layers directly exposed to the environment. One of the SNPs we have discovered is in a gene involved in determining the length of the telomeres, or the tail ends of chromosomes. Shorter telomeres have recently been linked to risk of certain cancers, and telomeres are known to become shorter with the accumulation of environmental insults over time. These findings may point us towards a means of addressing these risks by altering our lifestyle or by helping to identify targets for new drugs. We are integrating the SNPs into deCODEme™, and into our

deCODEme Cancer Scan™ launched today," said Kari Stefansson, CEO of deCODE and senior author on the paper.

deCODE discovered the first variant, a SNP called rs 401681, in its gene discovery work on basal cell carcinoma (BCC), a common form of skin cancer. The SNP is in the gene encoding cisplatin resistance related protein 9 (*CLPTM1L*). Because the region of chromosome 5p15 is of interest in cancer biology, the deCODE team then tested this SNP for association with 16 different types of cancer in a total of nearly 80,000 cancer patients and healthy control subjects from Iceland, the Netherlands, Italy, Sweden, Spain, Germany, Hungary, the United Kingdom, Belgium, Romania, Slovakia and the United States. Rs 401681 was found to confer increased risk not only of BCC, but also cancer of the lung, bladder, prostate and cervix, and was also found to protect against melanoma. It is of interest here that the risks of cancers of lung, bladder, prostate and cervix are greater in individuals with shorter telomeres than long, whereas those with long telomeres are at greater risk of melanoma. Through a more detailed analysis of this region, another SNP, rs2736089, was associated with increased risk of BCC and also with risk of cancer of the lung, bladder and prostate. Rs 2736089 is located in the gene encoding the human telomerase reverse transcriptase (*TERT*), which directs the addition of repeat DNA sequences to the ends of chromosomes. Importantly, the risk of these different cancers conferred by these two SNPs appears to be independent.

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