**IRON OVERLOAD
RAISES CANCER RISK**

Hereditary hemochromocytosis is caused by variants in the *HFE* gene that result in excessive absorption of dietary iron. As well as symptoms of iron overload, patients with this disorder often develop liver complications and diabetes. In a new study conducted in Australia, Nicholas Osborne and colleagues report that the most frequent *HFE* variant in patients with hereditary hemochromocytosis, which results in the amino-acid change Cys282Tyr, might also be associated with an increased risk of some types of cancer. "We found a doubling of the risk of diagnosis of colorectal and breast cancer in patients homozygous for this variant," comments Osborne. Interestingly, heterozygous individuals showed no increased risk. "Iron has long been thought to have toxic and carcinogenic effects," says Osborne. "So it was a plausible culprit."

A particular strength of the study was that it involved genotyping of DNA samples collected from 28,509 participants in the Melbourne Collaborative Cohort Study. These individuals were recruited without reference to the presence or absence of hemochromocytosis and before identification of the *HFE* gene, which reduced potential sources of bias. The study group included >4,000 carriers of the *HFE* mutation that results in Cys282Tyr, many more than previous studies were able to recruit. Incident cancer cases were ascertained from Australian cancer registry data.

"It would be fantastic to conduct research on whether it is high iron levels that are a risk factor for various cancers, rather than gene mutations linked to iron overload," notes Osborne. As the major source of iron in the body is dietary, he suggests that further studies should be conducted to examine this relationship more closely. "The ultimate goal would be establishing an intake level of iron that is safe for human lifetime exposure in relation to cancer risk," he concludes.

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Original article Osborne, N. J. *et al.* *HFE* C282Y homozygotes are at increased risk of breast and colorectal cancer. *Hepatology* 51, 1311–1318 (2010)