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PRESS RELEASE

Testosterone responsible for worsening iron overload in chronic liver diseases

A research team from Toulouse has just elucidated the mechanisms behind the differences in iron absorption between men and women. The team used mice to demonstrate how the action of testosterone can be "countered" with a drug already used in the treatment of some bronchial cancers. The results are published this month in the *Hepatology* review.

The regulation of the iron metabolism differs between men and women. As a consequence, chronic liver diseases associated with a reduced hepcidin production capacity - a hormone that inhibits iron absorption by the duodenum – are often more severe in men than in women.
This is the case for hepatitis C, alcoholic liver disease and hereditary hemochromatosis.
With a view to better understanding the underlying mechanisms of this sexual dimorphism, Marie-Paule Roth and her co-workers at the Centre for Physiopathology in Purpan (Mixed Inserm/CNRS/Université Paul Sabatier Research Unit, Toulouse) have taken advantage of the major differences in hepcidin expression and iron overload observed in male and female mice with iron metabolism disorders.
The researchers showed that testosterone robustly represses hepcidin transcription in these mice since it activates the growth factor receivers in the liver (EGF). Yet, when these EGF receivers are inhibited in male mice by a drug used in the treatment of some bronchial cancers, testosterone-induced repression ceases. Hepcidin production is then significantly increased. Castrating male mice leads to an increase in hepcidin production, as well as a very strong reduction in iron overload in the heart and pancreas of these mice.

To conclude, Marie-Paule Rothe and her team emphasise: "These results indicate that the testosterone-induced repression of hepcidin may have clinical repercussions for patients who, for different reasons, are only capable of producing hepcidin in limited quantities. Inhibiting the activation of EGF receivers in these patients could help them to produce more hepcidin, thus limiting iron overload that worsens the prognosis of chronic liver disease" they explain.

For further information

> Source

"Testosterone perturbs systemic iron balance through activation of EGFR signalling in the liver and repression of hepcidin"

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