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'Happy hour' gene discovery suggests cancer drugs might treat alcoholism

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A class of drugs already approved as cancer treatments might also help to beat alcohol addiction. That's the conclusion of a discovery in flies of a gene, dubbed happyhour, that has an important and previously unknown role in controlling the insects' response to alcohol.

Animals with a mutant version of the gene grow increasingly resistant to alcohol's sedative effects, the research shows. The researchers report further evidence that the gene normally does its work by blocking the so-called Epidermal Growth Factor (EGF) pathway. That EGF pathway is best known for its role in cancer, and drugs designed to inhibit the EGF receptor, including erlotinib (trade name Tarceva) and gefitinib (trade name Iressa), are FDA-approved for the treatment of non-small cell lung cancer.

Now, the researchers show that flies and mice treated with erlotinib also grow more sensitive to alcohol. What's more, rats given the cancer-fighting drug spontaneously consumed less alcohol when it was freely available to them. Their taste for another rewarding beverage -- sugar water -- was unaffected.

"This is a very powerful example of how simple model organisms -- and the little fruit fly in particular -- can be used to move quickly from an unknown gene to a potential therapy for drug addiction," said Ulrike Heberlein of the University of California, San Francisco, noting that erlotinib and gefitinib, along with other EGFR inhibitors, not only cross the blood-brain barrier in humans, but they are also well-tolerated in

general.

Alcohol is one of the most popular and abused drugs in the world, the researchers said. Therefore, a better understanding of the genetic and environmental factors that lead to its addiction would have considerable benefit for those who suffer its consequences and for society at large. Despite the well-known effects of alcohol consumption on behavior and cognition, the underlying basis for those effects on the nervous system are still rather incomplete.

Human studies have pointed to a strong genetic component to alcoholism, but identifying the specific genes responsible has proved difficult. Studies have also indicated that an individual's sensitivity to alcohol intoxication acts as a predictor of future alcoholism, with a link between lower initial response and increased risk of addiction. Therefore, Heberlein's team explained, genes and pathways involved in the acute response to alcohol can yield insight into the genetic factors contributing to the more complex process of addiction.

Earlier studies have shown that fruit flies are a useful tool for unraveling the basis for the effects of alcohol. Several genes previously identified as playing a role in fruit flies' alcohol response hold similar roles in mammals.

In search of more in the new study, the researchers screened mutant flies for those less sensitive to ethanol. That screen led them to happyhour, a gene closely related to mammalian enzymes known as the Ste20-family kinases of the GCK-1 subfamily.

Heberlein said they still don't know exactly how alcohol exerts its influence on the EGFR pathway or how that leads to the telltale changes in behavior that come with alcohol intoxication. Those questions will be the subject of future investigation. Her team is also exploring other new

gene candidates that turned up in the fly screens. She says that several of those appear to be tied to the EGFR pathway in different ways.

"It's not yet clear how it all fits together," she said. "But the fact that we've come, in an unbiased way, to molecules in the same pathway is telling us this is really, really important."

Source: Cell Press (news : web)