How Hobbs found a way to fight bad cholesterol

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Geneticist and her team discovered a rare mutation that protects against heart disease

- The discovery of cholesterol-lowering mutations in a human gene called PCSK9 led to the development of the most promising new drugs against heart disease since statins.
- Ms. Hobbs and her colleague at Dallas' UT Southwestern Medical Center, geneticist Jonathan Cohen, found that when people had a mutation in PCSK9, they ended up with lower levels of low-density lipoprotein (LDL) or bad cholesterol.
- Through this mechanism, the mutation protected people against heart disease, seemingly without side effects.
- In 2016, Ms. Hobbs was awarded the Breakthrough Prize in Life Sciences for her work.

PCSK-9 gene mutation

- The cue for which gene to focus on in the Dallas Heart Study came from a French study which found that people with familial hypercholesteremia – a genetic disorder leading to high LDL — tended to have a mutation in the PCSK-9 gene.
- The findings led to the development of the PCSK9 inhibitors Alirocumab and Evolocumab within 10 years, an unusually rapid example of drug development.
- The average time between the discovery of a drug target to commercialisation is typically 15 years.
- Today, Ms. Hobbs has turned her attention to fatty liver disease.
- Here, too, her efforts led to the identification of two gene mutations which promote the disease through different pathways.
- Both mutations increase triglycerides in blood through different mechanisms, while also making people susceptible to liver cirrhosis and

cancer.

- This finding shows that a condition called hepatic steatosis, in which fat builds up in the liver is not as benign as clinicians currently think, according to Ms. Hobbs.

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