

Genes on Y chromosome protect against pulmonary hypertension, study suggests

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A new UCLA study suggests that the Y chromosome provides protection against the development of pulmonary hypertension and may be the reason the disease is less prevalent among men than women. The researcher found that mice with Y chromosomes were significantly less likely to develop severe pulmonary hypertension than mice without Y chromosomes.

The findings suggest for the first time that sex chromosomes—not only sex hormones—may explain why women, who typically do not have a Y chromosome, are more susceptible to the <u>disease</u> than men.

Pulmonary hypertension, a chronic disease characterized by <u>high blood</u> <u>pressure</u> affecting the arteries and heart, appears most often in young women. It has no definitive cure and can be fatal. Many patients eventually require a lung transplant, a costly procedure that carries its own risks and requires a donor. Being male is the single biggest factor in avoiding development of <u>pulmonary hypertension</u>.

Previous studies have investigated sex hormones as a factor in the development of pulmonary hypertension. This study is the first to examine the involvement of sex chromosomes in the disease's development in the absence of sex hormones. In humans, females typically have two copies of the X chromosome, while males typically have one X and one Y chromosome.

In the lab, the researchers engineered mice with different chromosomal



makeups and measured their development of pulmonary hypertension in an environment with 10 percent oxygen, which is a well-established setting for inducing the disease.

One group of mice was engineered with sex chromosomes that were independent of their gonadal sex, or sex based on their genitalia, so that the researchers could isolate the impact of sex chromosomes. The other group of mice in the experiment had different variants of sex chromosomes in order for the researchers to determine the impact of the presence of a Y chromosome versus varying numbers of X chromosomes. All the mice had their gonads removed so that the researchers could eliminate the potential effects of sex hormones.

The researchers then placed the mice in the 10 percent oxygen environment for three weeks. At the end of the experiment, the researchers examined the hearts and lungs of the mice. Mice with a Y chromosome experienced significantly less severe pulmonary hypertension and were protected against the development of the disease.

These findings identify a new avenue for research into effective ways to treat pulmonary hypertension. In the future, determining which genes on the Y chromosome confer protection will be vital and could lead to novel therapies for the disease.

The disease causes extreme distress to patients as well as their families. Identifying alternative, less invasive treatments would be an important step in combatting the disease, which affects hundreds of thousands of people in the United States alone, according to the American Thoracic Society.

More information: Soban Umar et al. The Y Chromosome Plays a Protective Role in Experimental Hypoxic Pulmonary Hypertension, *American Journal of Respiratory and Critical Care Medicine* (2017).



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