

Got to go? Harvard scientists figure out how you know

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If you have an overactive bladder or incontinence, help could be on the way. A new research report published online in the *FASEB Journal*, shows that the epithelium, a thin layer of cells which line the surface of the bladder, is able to sense how full the bladder is through the action of a family of proteins called integrins. As the bladder becomes full, the cells in the epithelium stretch and become thinner, which activates the integrins to send that information to nerves and other cells in the bladder. As a result of this new knowledge, researchers may one day be able to design drugs that target this mechanism to treat conditions like incontinence and overactive bladder, both of which are common, serious, problems affecting millions of people.

"I am very hopeful that as we learn more about how the bladder senses fullness and conveys that information to the nerves and the muscles which control our ability to urinate, that this greater understanding and knowledge will lead to new treatments," said Warren G. Hill, Ph.D., a researcher involved in the work from the Department of Medicine at Beth Israel Deaconess Medical Center and Harvard Medical School in Boston, MA. "It is extremely important that we do this as quickly as possible, since there are millions of people who suffer enormously from the anguish of [bladder pain](#), incontinence and constant feelings of needing to go. I am optimistic these new insights into the role of integrins will begin the process of discovering important new [drug targets](#) which will dramatically improve the quality of life for many of these people."

To make this discovery, Hill and colleagues tested two groups of mice. The first were genetically modified to not have an important member of the integrin family present in the [epithelium](#). The second group of mice was normal. The mice lacking the integrin protein had normal looking bladders but very little urinary control. The normal mice also had normal looking bladders, but as expected, had [bladder control](#). Researchers then tested the bladders from the integrin knockout mice and found that their bladders were constantly squeezing and very overactive. In addition, they overfilled their bladders and took much longer to urinate than the normal mice. Since most drug treatments for [overactive bladder](#) target proteins in the muscle surrounding the bladder, this study shows that it may be possible to design drugs that target sensory proteins in the epithelium.

"No one wants to pee in his or her pants," said Gerald Weissmann, M.D., Editor-in-Chief of the [FASEB Journal](#), "but the reality is that bladder problems – incontinence, frequency and pain - affect more people than we realize. This report offers hope that new drugs targeting the [bladder's](#) epithelium will succeed when current drugs fail."

More information: Keizo Kanasaki, Weiqun Yu, Maximilian von Bodungen, John D. Larigakis, Megumi Kanasaki, Francisco Ayala de la Pena, Raghu Kalluri, and Warren G. Hill. Loss of β 1-integrin from urothelium results in overactive bladder and incontinence in mice: a mechanosensory rather than structural phenotype. *FASEB J* [doi:10.1096/fj.12-223404](https://doi.org/10.1096/fj.12-223404)

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