

# Scientists discover new drug candidates for cystic fibrosis and other diseases

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A new discovery by Californian scientists may lead to a pharmaceutical breakthrough for a wide range of illnesses that involve the hydration of cells that line the inner surfaces of our body's organs and tissues. In a new report appearing in the *FASEB Journal*, the researchers describe how they used high-throughput screening to identify small-molecule drug candidates which help cells bypass defective channels that normally move salt and water through cell membranes. These drug candidates work by activating an alternative chloride channel called "TMEM16A" that might be effective in treating conditions such as cystic fibrosis, dry eye and dry mouth diseases and slow-transit constipation.

"Further pre-clinical development of the [chloride channel](#) activators identified in our study may lead to new drug therapies for [cystic fibrosis](#), dry eye and mouth syndromes, and certain types of constipation," said Alan S. Verkman, M.D., Ph.D., study author from the Department of Medicine at the University of California, San Francisco.

Verkman and colleagues discovered these compounds by using high-throughput screening, in which more than 100,000 drug-like compounds were tested for their ability to activate the TMEM16A channel. Active compounds coming from the screen were further improved and tested in cell and mouse models. These compounds were found to help facilitate salt and water movement, making them promising drug candidates.

"Scientists have known for decades that cells have more than one way to move salt and water. Indeed, over the years many useful drugs have been

developed that influence these movements in the heart and kidneys," said Gerald Weissmann, M.D., Editor-in-Chief of the [FASEB Journal](#). "This discovery is important not only because it identifies a new channel present all over the body, but finds a promising agent to activate it. As further drug candidates are devised to target TMEM16A, this work may lead to clinical advances of major significance."

**More information:** Wan Namkung, Zhen Yao, Walter E. Finkbeiner, and A. S. Verkman. Small-molecule activators of TMEM16A, a calcium-activated chloride channel, stimulate epithelial chloride secretion and intestinal contraction. *FASEB J.* November 2011 25:4048-4062; [doi:10.1096/fj.11-191627](https://doi.org/10.1096/fj.11-191627)

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