Old drugs learn new tricks: drug repurposing saves the world!

New way of drug discovery, “drug repurposing” has come into the spotlight. Drug repurposing—also known as drug reprofiling or drug repositioning—is essentially using “old” drugs to treat “new” diseases. With increases in knowledge about the molecular mechanisms underlying diseases, drug repurposing has emerged as a new strategy that involves using existing drugs originally developed for one disease to treat another disease. Thus, the time required for drug development is shorter, since preclinical and most clinical drug-safety trials can be skipped for an already-approved drug. With drug repurposing: That old drug used to treat “disease A” can be used for a new purpose—to treat “disease B.”

Medicines that are no longer used for their initial purpose regain their utility surprisingly as new medicines to treat new diseases. Examples include using thalidomide to treat multiple myeloma, chloloquine to treat autoimmune diseases, and chinoform to treat dementia and autism. This strategy has become very valuable in recent years, as drug pipelines of pharmaceutical industries have continued to dry up. In addition, pharmaceutical companies realize that many previously promising compounds fail to generate medicines for their intended uses. So why not use them for another purpose? That is, use them to treat other diseases that share similar biological pathways and molecular mechanisms.

The cAMP pathway is a microscopic biological signaling pathway used in cell-to-cell communication in the body. This pathway is necessary for many living organisms and life processes. cAMP comes into play during cellular processes responsible for heart rate, cortisol secretion, water absorption in the kidney, and breakdown of metabolic energy sources and fat, among others. cAMP is also crucial for memory functions in many species of animals. A recent approach to modulate the cAMP pathway is to maintain and/or prolong the “on site” cAMP effect induced by memory-related neuronal activity. For this purpose, enzymes called phosphodiesterases (PDEs) have been targeted for memory enhancement and maintenance, since they are important for adjusting cAMP levels in the body.

Inhibition of PDEs leads to increases in cAMP and ultimately to the expression of plasticity-related genes involved in memory. We discovered in our lab that cilostazol also beneficially affects memory function. Cilostazol is a specific PDE3 inhibitor and has been on the market for decades to prevent recurrent strokes and to treat intermittent leg cramping. Recently, we showed that cilostazol enhances memory in young mice in spatial memory task and in Pavlovian conditioning. More importantly, we showed that long-term administration of cilostazol significantly improves memory in very old mice. Might cilostazol help older adults with memory problems?

Other lab’s works and ours’ have further demonstrated the effectiveness of cilostazol and other PDE inhibitors for enhancing memory. Now, cilostazol is being tested in a clinical trial to treat mild

cognitive impairment, which in people is marked by memory problems.

Like the old dog that has learned a new trick, cilostazol learns a new trick and may be available at your prescription counter to treat memory problems, thanks to drug repurposing, a quicker and safer way for drug discovery.

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Publication

Long-term cilostazol administration ameliorates memory decline in senescence-accelerated mouse prone 8 (SAMP8) through a dual effect on cAMP and blood-brain barrier.
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