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In This Issue

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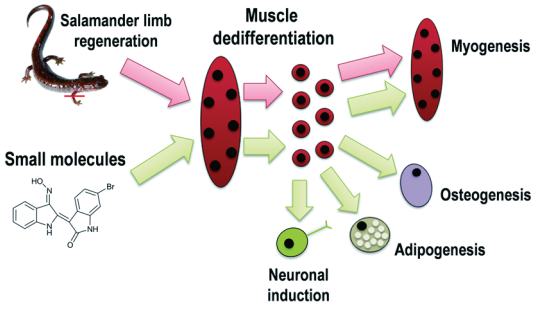
A NEWT METHOD FOR TISSUE REGENERATION

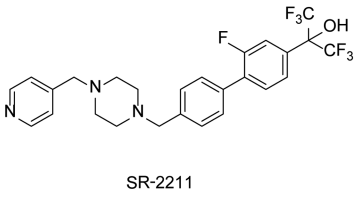
Urodele amphibians, such as salamanders and newts, have the extraordinary ability to regenerate their limbs, and understanding this process better could have profound implications for tissue repair and organ regeneration in humans. A key initial event in limb regeneration in amphibians is the conversion of the muscle cells near the site of injury to a special state from which they can develop into the different cell types necessary to generate new tissue. Small molecules that could induce similar changes in mammalian muscle cells have much therapeutic promise in regenerative medicine. Kim *et al.* (DOI: 10.1021/cb200532v) now report the identification of four small molecules that promote the growth of new cell types from mammalian muscle cells.



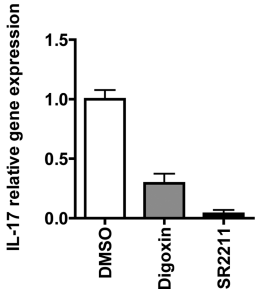
The four molecules, called lysophosphatidic acid, SQ22536, SB203580, and BIO, are known modulators of various cellular signaling pathways. Specially prepared mouse muscle cells treated with these compounds became capable of turning into new muscle cell types as well as other cell types such as precursors to fat, bone, and nervous system cells.

INTERFERING WITH AN INTERLEUKIN

The retinoic acid-related orphan receptor γ (RORγ) is a nuclear receptor that controls production of a protein called interleukin 17 (IL-17), which is involved in the inflammatory response, and the differentiation of Th17 cells, which have been implicated in several autoimmune diseases including multiple sclerosis and rheumatoid arthritis. The natural ligands for RORγ are controversial, but evidence suggests that modulators of this receptor that diminish IL-17 expression could have therapeutic potential. Kumar *et al.* (DOI: 10.1021/cb200496y) now report the design and activity of a selective small molecule RORγ modulator called SR2211.



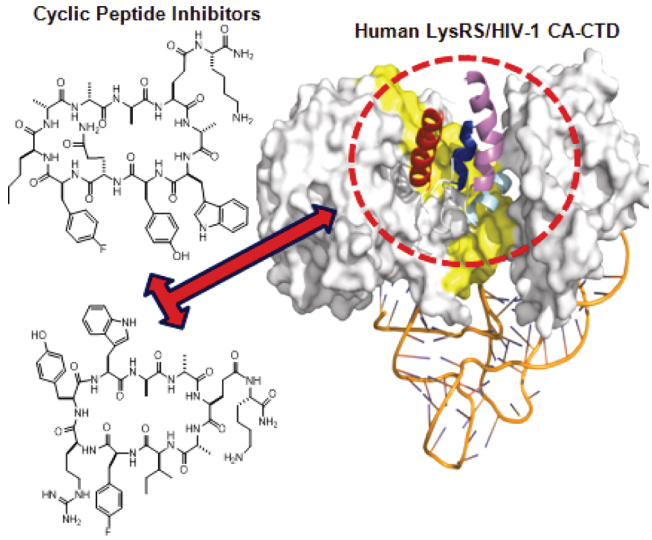
SR-2211



The structure of SR2211 was inspired by another small molecule SR1001, which is a RORγ modulator that also binds to a related receptor. By tweaking the structure activity relationships in the compound, the authors were able to create a selective RORγ modulator. Binding experiments confirmed that SR2211 interacted directly with RORγ, and experiments in cells demonstrated that it is a potent inhibitor of IL-17 production. Together, the data suggest the potential therapeutic utility of SR2211 for autoimmune disorders.

CORRALLING THE CAPSID PROTEIN

Human immunodeficiency virus type 1 (HIV-1) relies on key proteins, such as HIV protease and reverse transcriptase, to replicate and thrive. While drugs targeting these proteins have been relatively successful at keeping the virus at bay, the emergence of strains resistant to them precludes our ability to fully eradicate the virus. Development of drugs targeting other proteins crucial to the viral life cycle is an attractive strategy for combating drug-resistant strains. Dewan *et al.* (DOI: 10.1021/cb200450w) now report their approach for targeting the capsid protein, a viral protein involved in numerous important processes including reverse transcription.



The authors designed and synthesized a library of cyclic peptides and screened them for their ability to bind to the capsid protein. They identified several cyclic peptides that inhibited the interaction between the capsid protein and human lysyl-tRNA synthetase, which facilitates the reverse transcription process. These novel compounds are exciting jumping off points for development of a new class of anti-HIV-1 therapeutics.

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