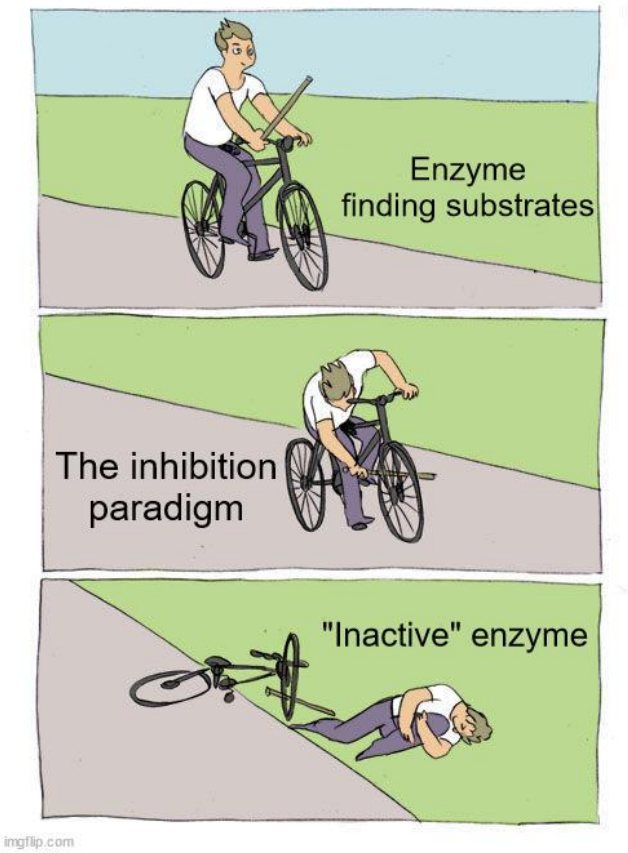
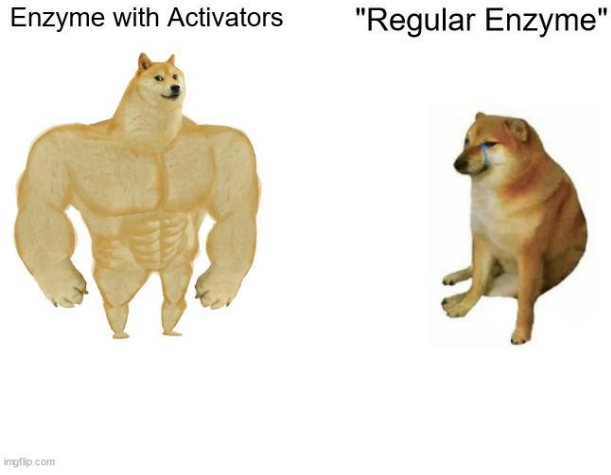
A new modulator class

OGG1 activators work in a complex way to carry out their function. In this context, we utilize a variety of popular Memes from pop-culture to effectively communicate the key principles to non-experts.



1. When it comes to targeting enzymes, pharmacological modulators can function as either inhibitors or activators. Inhibitors work by blocking the active site of the enzyme, which prevents the binding of substrates and, consequently, hinders the enzyme's function. Alternatively, they can bind to a different site on the enzyme, causing a change in its three-dimensional structure and achieving a similar outcome. In order to effectively block the function of all copies of the enzyme and achieve a desired therapeutic effect, relatively high concentrations of the inhibitor are usually required. Ideally, once an inhibitor is bound to the enzyme, it remains there for an extended period of time.



2. Activators of enzymatic function work by binding to a remote site on the enzyme, causing a change in the enzyme's three-dimensional structure. This structural alteration leads to enhanced substrate binding or increased efficiency in product unbinding. It is important to note that activators should not bind to the active site of the enzyme, as that would compete with the substrate and act as inhibitors instead. Activators often govern highly effective enzymes, surpassing the performance of non-activated copies.

Achieving stability in a specific three-dimensional structure may take some time for the enzyme, but once it is achieved, the activators typically remain associated with the protein. As a result, relatively high concentrations of activators are needed to achieve the desired therapeutic effect.

3. OGG1 activators belong to a novel category of activators known as organocatalysts. Organocatalysts are small synthetic molecules that do not contain any metal components and are composed solely of elements commonly found in organic systems, such as nitrogen, oxygen, hydrogen, carbon, and halides. They possess an active center or atom within their molecular structure that enables specific chemical transformations. Importantly, catalysts remain unchanged after a transformation and can be reused.

In the case of OGG1, organocatalysts serve as chemical bases by abstracting a proton. Nitrogen, present in many organocatalysts, can efficiently exchange protons with its surroundings. These compounds target the DNA repair intermediate of OGG1, combining protein affinity with the active center nitrogen. Since the organocatalyst remains unaltered during the reaction, it can activate multiple enzyme copies in succession. Consequently, OGG1 activation can be achieved even at very low concentrations of the organocatalyst compound.

4. The intermediate that is targeted by OGG1 activators is typically not cleaved by the OGG1 enzyme alone. Instead, a second enzyme is recruited to carry out this particular step. However, by utilizing small molecules as activators instead of another enzyme, the time required for these reactions is significantly reduced. The cleavage of the intermediate becomes highly efficient and is no longer the step that limits the overall rate of DNA repair for 8-oxoguanine (8-oxoG).

5. The primary enzymatic function of OGG1 is to remove the damaged nucleobase 8-oxoguanine from DNA. However, enzymes often possess additional enzymatic activities that are either lost during evolution or have become redundant over time. In the case of OGG1, the cleavage of the intermediate mentioned earlier is one such rudimentary enzymatic activity.

By utilizing OGG1 activators, the cleavage of this intermediate is accelerated, resulting in a new enzymatic function for OGG1. In this altered function, OGG1 prefers to resolve the intermediate (abasic sites) rather than repairing 8-oxoguanine directly. Since abasic sites are more abundant in cells compared to 8-oxoguanine, this rewires the enzyme's role in DNA repair.

6. Proton abstraction in the DNA intermediate during the OGG1 activation process can result in various reaction products. By carefully selecting specific OGG1 activators, it becomes possible to control the ratio of these products according to desired outcomes.

However, it's important to consider the potential consequences of artificially accelerating DNA repair. When DNA repair products are generated at an accelerated rate, it may overwhelm the cell with toxic DNA damage intermediates. This can pose a challenge for the cell to handle and may have detrimental effects on its overall function. Then, this DNA damage overload can be beneficial in the treatment of cancer, where cancer cells rely on an efficient repair more than healthy cells.

Conversely, in situations where a cell is struggling to effectively repair DNA damage, accelerating the DNA repair process can be an appealing approach to reduce the levels of such damage. By enhancing the efficiency of DNA repair, it becomes a potential avenue to alleviate the burden of DNA damage within the cell.

It is important to note, that both applications are possible for OGG1 activators. More research is necessary to find the right dose and establish intervention protocols for each indication.