

Picking the best isoform

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STATEMENTS

Picking the best isoform

PDE4D isoforms as therapeutic targets in Alzheimer's disease

Dean Paes

1. If a gene encodes multiple protein isoforms, it very likely does so for a good reason.
2. Targeting specific rather than all PDE4D isoforms will be therapeutically superior in treating memory problems associated with Alzheimer's disease.
3. Synergistic actions of PDE4 and PDE2 inhibition should be explored as an effective and safe treatment strategy for treating memory deficits in Alzheimer's disease.
4. Measuring the affinity of a PDE4 inhibitor is highly dependent on the sequence and the conformational state of the PDE4 construct used, of which the latter is dependent on the type of assay used.
5. Drug development efforts should focus on the target in its native state(s) rather than screening compounds in cell-free assays using truncated target constructs.
6. Cell culture experiments should be complemented with computational biology approaches to reveal some of the complex non-linear dynamics in the otherwise 'black box'.
7. The best interventions for Alzheimer's disease may be those applied before its onset.
8. Target specification to the level of protein isoforms can improve therapeutic efficacy and, therefore, should be explored for any pharmacological target for any disease.
9. Life is nothing but an electron looking for a place to rest.
- *Albert Szent-Györgyi*
10. Knowledge isn't free. You have to pay attention.
- *Richard Feynman*
11. βούλεσθαι μᾶλλον μίαν εὐρεῖν αἰτιολογίαν ἢ τὴν Περσῶν οἰ βασιλείαν γενέσθαι
(I would rather discover one true cause than gain the kingdom of Persia.)
- *Democritus*