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## A clinical and translational research view on Alzheimer disease therapeutics

Alzheimer's disease is the most important epidemic of the 21st century. Its rising medical, psychosocial and economic burden is to the extent that our society will need to deal, and perhaps change our moral attitudes on issues of end-of-life decisions.

The main problem hindering the development of therapies is the lack of early diagnosis. This is due to that at the earliest clinical presentation of mild cognitive impairment (MCI) there is already significant irreversible brain damage. Therefore, clearly, diagnosis needs to be done at a pre-clinical stage.

It does not seem realistic to regenerate the brain in the foreseeable future. Our aims are to prevent (or delay onset) the disease and to slow down its progression. Delaying disease onset by average of just 10 years will have a dramatic impact.

From the medical and socio-economic point of view the main problem in current developments in the field are probably the cost of diagnosis and treatment. Amyloid PET scans provide a useful tool to identify patients at risk, but their cost makes them not practical for repeated wide population based screenings. The emerging anti-Amyloid drugs have failed so far mainly due to treatment at a stage of full-blown Alzheimer's disease rather than at the point of shift from the pre-clinical to clinical phase. Furthermore, the costs of therapy will leave them as drugs for the rich. Therefore, a solution is needed in the current Pharma-dependent drug development system, which is biased towards development of blockbuster drugs.

I will present several alternative solutions from my own scientific milieu:

1. An easy-to-use, rapid and inexpensive evaluation that can detect the earliest cognitive change in pre-clinical stages of Alzheimer's disease. This can be delivered to the wide population through internet (smartphone application) and serve as screening before PET imaging and further evaluations.
2. Approaches to develop safe and inexpensive compounds to protect the brain that can be distributed to the wide ageing population. Examples are powerful anti-oxidants that do indeed reach and affect the brain, and modulating the toxicity of microglia and protective effect of brain stem cells, as key players in generative a healthy brain environment.

Finally, I will suggest a "teaser" on the much-needed symptomatic treatment for patients with full-blown Alzheimer's disease. In particular, I will provide some experimental and clinical indications on reversible memory deficits and the role of treatable inflammatory mediators.

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