Alzheimer’s disease (AD) is an irreversible, neurodegenerative disease, without current therapies that can stop the development of AD [1,2]. The last two decades have brought forth compelling new findings showing that cell cycle re-entry in mature neurons is an early and consistent feature of AD, manifested as over-expression of cell cycle related molecules, DNA replication, and subsequent neuronal death [3-8].

The mature neuron that re-enters the cell cycle can neither advance to a new G0 quiescent state (since the neuron is unable to get through mitotic phase and divide), nor revert to its earlier G0 state (since the cell cycle is an irreversible cellular process) [9]. This critical dilemma to the cycling neurons presents a possible mechanism by which aberrant cell cycle re-entry results in post-mitotic death of neurons. In contrast, the aberrant cell cycle contributes to uncontrolled proliferation of cancer cells.

Some pharmacological agents (e.g., flavopiridol, everolimus, rapamycin) that interfere with cell cycle have been used in clinic or clinical trials for cancer therapies [9]. These agents have also been examined to protect neurons in animal AD models [9], though not advanced for clinical trials in treatment of AD yet. By contrast, the drugs that are used for treating AD in clinic (e.g., memantine, donepezil) are also able to block cell cycle [10]. Therefore, the two seemingly unrelated disease types (AD and cancers) may share the common mechanism: aberrant cell cycle re-entry, as the same approach of cell cycle inhibition can treat both AD and cancers.

One recent study indicates that transgenic AD mice have increased risk to develop brain tumors than wild-type controls, when they are exposed to carcinogen methylcholanthrene [11]. However, epidemiological study shows that AD patients have reduced risk of cancers [12]. It is likely that the drugs that AD patients receive may prevent carcinogenesis through cell cycle arrest. Since the mere entrance into the initial cell cycle may lead to unavoidable cell death of neurons, the best strategy appears to prevent neurons from leaving G0 phase via targeting upstream mitogenic pathways prior to the G0/G1 transition - the first step of cell cycle.

REFERENCES