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Stem Cells as a Target of Prophylactic Pharmacology

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Abstract

Stem cells are primitive immature cells endowed to proliferate for replication along with differentiation to particular progeny cellular lineages. Pharmaceutical drugs have been used for improvements of different symptoms caused by consequential accumulation of a variety of dysfunctions of both tissues and organs composed of mature cells after differentiation in patients as the therapy and treatment with inevitable side effects. By contrast, prior alleviation of cellular dysfunctions seems more important and reasonable at the level of stem cells as a prophylactic strategy than the therapy after the onset of illness.

Introduction

Our body is believed to be composed of 40 trillions of different types of eukaryotic cells which are all originally derived from one single Embryonic Stem (ES) cell. The ES cell is of course unable to proliferate for self-renewal itself, but endowed to differentiate into a variety of primitive stem cells capable of proliferating for self-replication and differentiating into discrete progeny cell lineages. Frequent repetition of these proliferation and differentiation processes is responsible for the commitment to different progenitor cells toward subsequent functional orchestration by destined cells to tissues, organs, systems and individuals. Sustained malfunctions of particular cellular molecules would thus induce abnormalities and dysfunctions of cells and tissues, which undoubtedly lead to the consequential crisis of various symptoms and syndromes seen in patients with particular diseases. Qualified beneficial effects have been brought about by the acute administration of medicines and drugs for amelioration of different syndromes and symptoms in patients suffering from a variety of diseases and disorders at the cost of untoward side effects sometimes highly toxic.

Prophylaxis by nutraceuticals

By contrast, sustained intake of edible materials has been believed to be clinically useful for the prophylaxis and/or alleviation of unpleasant conditions in people with particular health disturbances. These include dietary supplements and nutraceuticals mainly derived from edible foods, traditional medicines and herbal extracts. Although numerous edible materials have been used with secured safety for alleviation of unpleasant disabilities attributable to cellular malfunctions in young and elderly people for hundreds of years, validated evidence is fatally absent from the literature relevant to the usefulness and effectiveness with clarified underlying mechanisms in edible health beneficial materials. Oral administration of drugs could induce acute and effective improvement of different symptoms in patients with a particular disease. However, sustained oral intake would be required for the realization of beneficial alleviations of unpleasant disabilities by dietary supplements and nutraceuticals in people without diagnosed diseases. These facts argue in favor of an idea that people would prefer edible nutraceuticals with secured safety for the prophylaxis rather than pharmaceuticals with possible severe side effects for the therapy in any disabled situations. As mentioned above, however, mechanisms underlying the protection of cellular abnormalities are mostly unclarified with dietary supplements and nutraceuticals compared to pharmaceuticals so far. Prophylaxis by nutraceuticals would let the people avoid any unpleasant symptoms due to malfunctioned cells, tissues and organs. Apart from an economical point of view, we should accumulate a body of scientifically verified evidence for the usefulness and effectiveness along with guaranteed safety and clarified mechanism for the beneficial alleviations by dietary supplements and nutraceuticals as quickly as possible.

Accelerated neurogenesis by the green tea amino acid theanine

From this viewpoint, I would introduce our experimental results on the improvement mediated by facilitated neurogenesis of brain dysfunctions after sustained oral intake of the green tea amino acid L-theanine. L-Theanine is an exogenous amino acid detected in green tea with a structural analogy to several neuro active endogenous amino acids such as L-glutamine (Gln) and L-glutamic

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acid [1]. We studied pharmacological features of this green tea amino acid highly relevant to Glnrather than L-glutamic acid in neural progenitor cells capable of proliferating for self-replication and differentiating into neuronal, astroglial and oligodendroglial lineages in embryonic, developing and adult brains. Markedly significant alleviation was found in the cognition ability score assessed by double-blinded expertise physicians in healthy elderly age-matched people with capsules of powdered green tea enriched of L-theanine compared to those with normal green tea powder capsules after daily oral intake for 7 to 12 consecutive months. Daily oral intake of L-theanine prevented the decline of 5-bromo-2'-deoxyuridine incorporation in the hippocampal dentate gyrus together with amelioration of behavioral abnormalities in adult mice with traumatic stress [2]. In cultured neural progenitor cells isolated from embryonic rodent cortices, L-theanine promoted proliferation and subsequent neuronal differentiation, along with deteriorated astroglial differentiation [3]. In cultured progenitor cells from the hippocampus of adult nestin-green fluorescent protein mice, moreover, sustained exposure to L-theanine led to the increased size of neurospheres composed of clustered proliferating cells. In murine embryonic carcinoma P19 cells which are more primitive than neural progenitor cells, similar promotion was seen in proliferation and neuronal differentiation after exposure to L-theanine. Exposure to L-theanine for a rather long time up-regulated the Gln transporter *Slc38a1* transcript expression in rat and mouse progenitors, while stable overexpression of *Slc38a1* drastically facilitated both proliferation and neuronal differentiation in pluripotent P19 cells [4]. However, L-theanine failed to further promote both proliferation and neuronal differentiation in P19 cells stably overexpressing *Slc38a1*. Moreover, marked phosphorylation was seen with mammalian target of rapamycin (mTOR) and downstream proteins in murine neural progenitors and pluripotent P19 cells with sustained exposure to L-theanine [5]. On the basis of the findings described above, we proposed that L-theanine may be endowed to promote embryonic and adult neurogenesis from neural progenitor cells in a manner associated with upregulation of the Gln transporter Slc38a1 for activation of intracellular mTOR signaling in rodent brains [6].

Future Trends

As such I would like to emphasize the crucial importance of laboratory experiments using molecular and cellular biological techniques as done with pharmaceuticals to provide validated evidence for the effectiveness of dietary supplements and nutraceuticals clinically beneficial for the prophylaxis and alleviation of a variety of unpleasant symptoms derived from cellular dysfunctions in people without particular diseases diagnosed. In association with pharmaceutical sciences, finally, clinical intervention and cohort trials are also acceptable and appreciable for the urgent establishment of nutraceutical sciences, in addition to pharmacokinetics and pharmacodynamics.

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