جامعة الملك عبدالله
للعلوم والتقنية
King Abdullah University of
Science and Technology

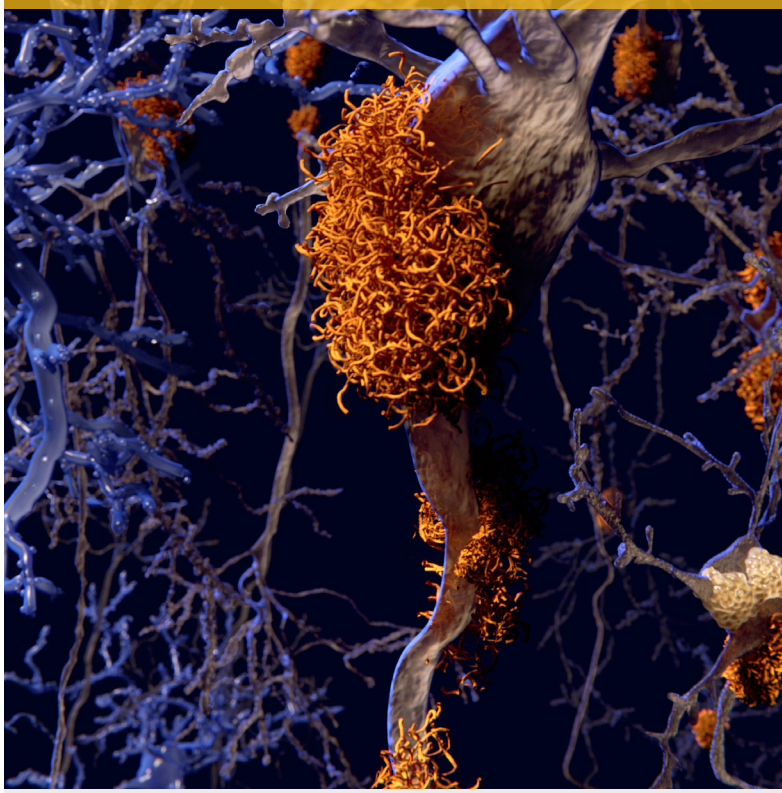
Combinatorial Drugs for Treatment of Alzheimer's Disease and other Neurodegenerative Disorders

Drug candidates to inhibit the progression of neurodegenerative disorders

KAUST researchers have identified Parthenolide in combination with other well-known and characterized compounds as potential inhibitors of known pathways involved in the pathogenesis of Alzheimer's disease. Advanced bioinformatics analysis reveals significant potential for Parthenolide to decrease the expression of six molecules (IkappaBα, NF-κB, NO, iNOS, TNFα, and IL-1β) associated with Alzheimer's. The findings indicate that the major inflammatory pathways leading to the disease progression could be blocked when Parthenolide is used in combination with inhibitors of the tri-molecular receptor complex (TLR4/MD-2/CD14), such as Curcumin or Resatorvid, to reduce the processing and activation of caspase -8 and -3. The use of nACHR agonists such as Tilorone was also indicated to help restore normal cellular processes.

These combinations represent an opportunity to change the progression of Alzheimer's disease whereas current drugs merely treat the disease's symptoms. In addition, the compounds identified by the bioinformatics analysis at KAUST hold potential for treatment of other neurodegenerative diseases, such as Parkinson's and Huntington's.

TECHNOLOGY OPPORTUNITY



Benefits

- **Attacks the Source:** Potential to inhibit the major known inflammation pathways that cause neurodegenerative disease
- **Therapeutic, not Palliative:** Changes the progression of neurodegenerative diseases instead of only treating the symptoms
- **Established Compounds:** The proposed combinations employ compounds that are well-known and extensively characterized by the scientific community

Applications

- Alzheimer's disease
- Parkinson's disease
- Multiple Sclerosis
- Huntington's disease
- Prion diseases

Opportunity

This technology is part of KAUST's technology commercialization program that seeks to stimulate development and commercial use of KAUST-developed technologies.

Opportunities exist for joint development, patent licensing, or other mutually beneficial relationships.

For More Information

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Technology Details

Molecule	Expression in Alzheimer's Disease	Expression Effect with Parthenolide	Expression Effect with with Tri-Molecular Inhibitors
IkappaBα[1]	↑	↓	n/a
NF-κB[1]	↑	↓	n/a
NO[2]	↑	↓	n/a
iNOS[2]	↑	↓	n/a
TNFα[1]	↑	↓	n/a
IL-1β[1]	↑	↓	n/a
TRL4[3]	↑	n/a	↓
MD-2[4]	↑	n/a	↓
CASP8[3]	↑	n/a	↓
CASP3[3]	↑	n/a	↓

- *1 Saadane, A., Masters, S., DiDonato, J., Li, J. & Berger, M. (2007) Parthenolide inhibits IkappaB kinase, NF-kappaB activation, and inflammatory response in cystic fibrosis cells and mice. Am J Respir Cell Mol Biol, 36, 728-736.*
- *2 Fiebich, B.L., Lieb, K., Engels, S. & Heinrich, M. (2002) Inhibition of LPS-induced p42/44 MAP kinase activation and iNOS/NO synthesis by parthenolide in rat primary microglial cells. J Neuroimmunol, 132, 18-24.3*
- *3 Burguillos, M.A., Deierborg, T., Kavanagh, E., Persson, A., Hajji, N., Garcia-Quintanilla, A., Cano, J., Brundin, P., Englund, E., Venero, J.L. & Joseph, B. (2011) Caspase signalling controls microglia activation and neurotoxicity. Nature, 472, 319-324.*
- *4 Gradisar, H., Keber, M.M., Pristovsek, P. & Jerala, R. (2007) MD-2 as the target of curcumin in the inhibition of response to LPS. J Leukoc Biol, 82, 968-974.*

The combination of Parthenolide with inhibitors of the tri-molecular receptor complex hold great potential to inhibit the major pathways that causeAlzheimer's disease (above).

IP Protection

KAUST has a patent pending for this technology.

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