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GENUV

Trametinib restores memory deficits by activating endogenous neurogenesis in mouse model of Alzheimer's disease

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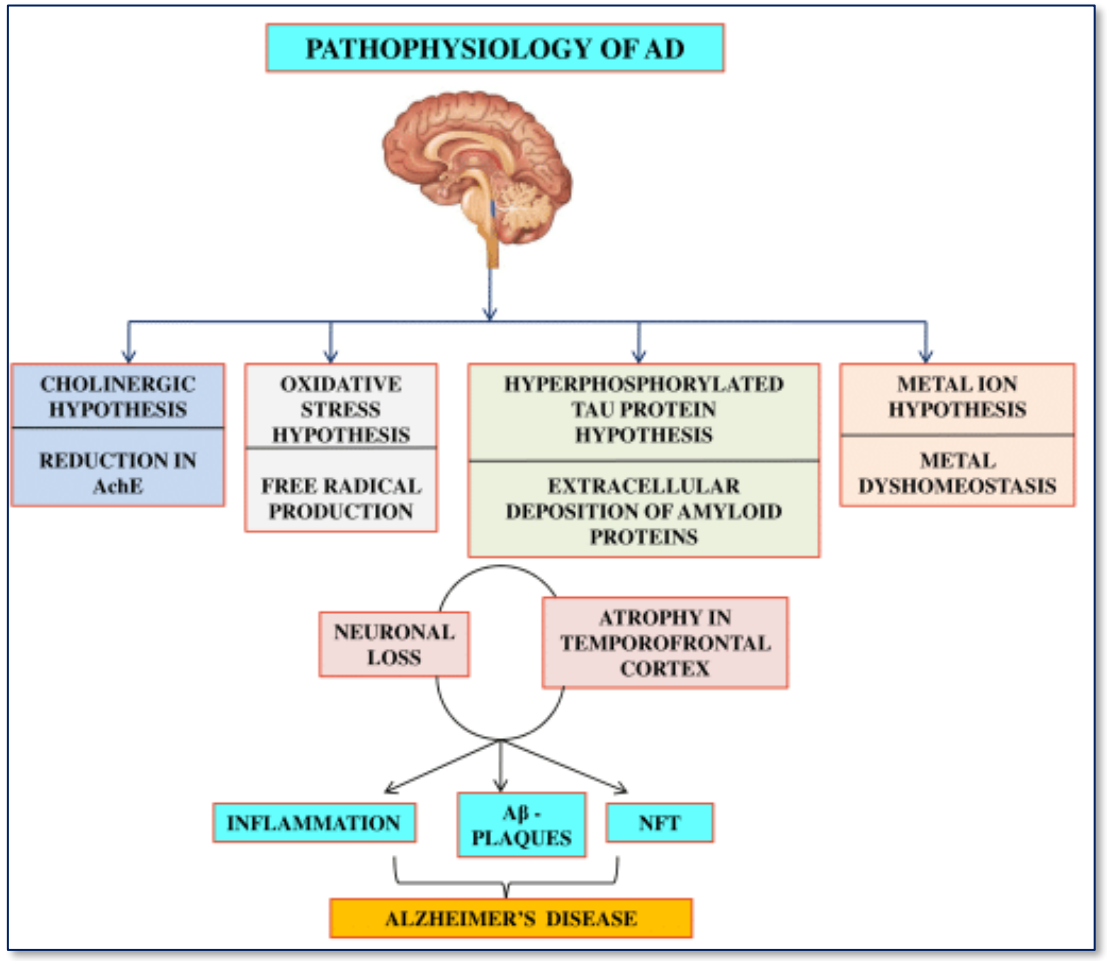
Scientific Imagination for a Healthier Future

Alzheimer’s disease



J Anal Pharm Res. 2018;9(2):226-235

- **Progressive neurodegenerative disease**
  : Cognitive impairment and functional decline
- **Pathological hallmarks**
  : Amyloid plaques & fibrillary tangles
  : Neuronal loss in the brain
- **Pathophysiological factors**
  : Cholinergic dysfunction
  : Amyloid/tau toxicity
  : Oxidative stress/mitochondrial dysfunction etc.

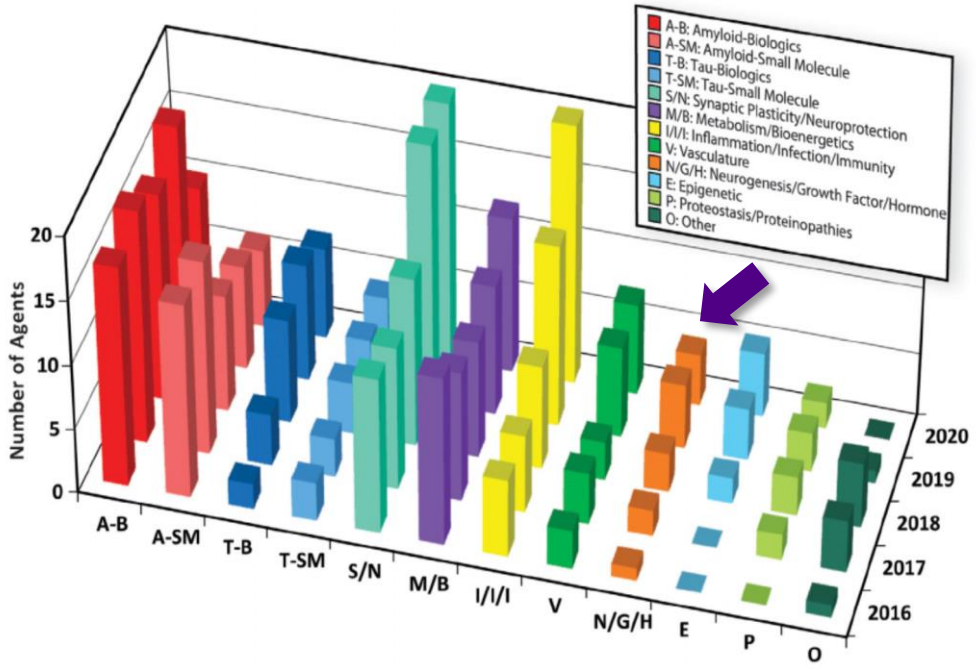
Drug development for AD

- Decrement of amyloid target drug development
- Already damaged neurons are very difficult to regenerate

⇒ It is necessary to change the idea of the development strategy

New strategy AD drug development

: Enhancing endogenous neurogenesis

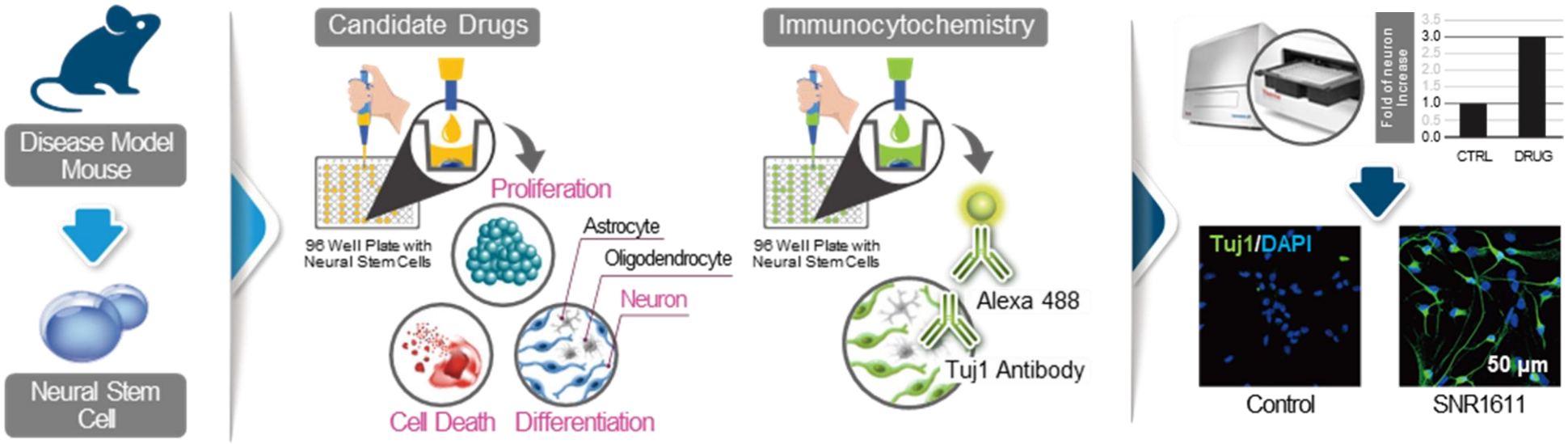


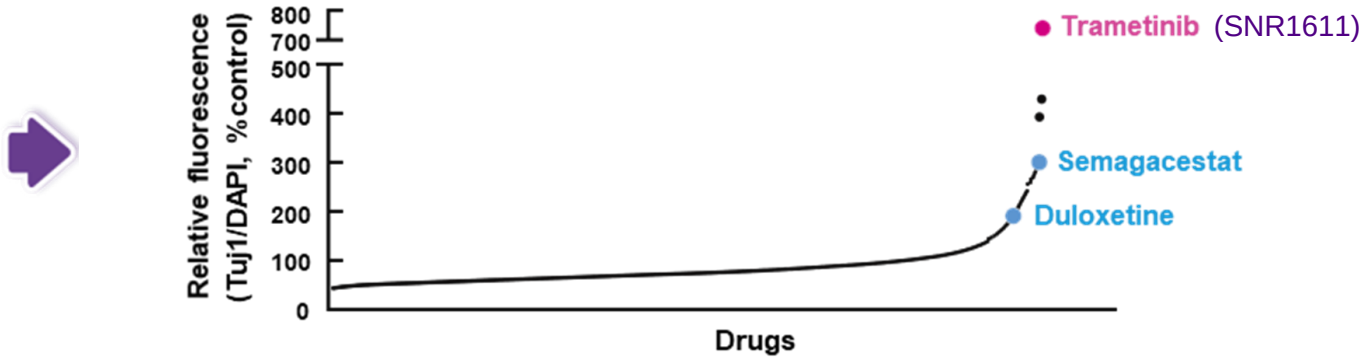
Alzheimers Dement (N Y). 2020 Jul 16;6(1):e12050.

DRUG SCREENING by ATRIVIEW®

NO – PHOTO / RECORD

- **Identifying Novel Target(S) and Drug Candidate(s) – Neurogenesis / Adult Neural Stem Cells from AD model mouse**



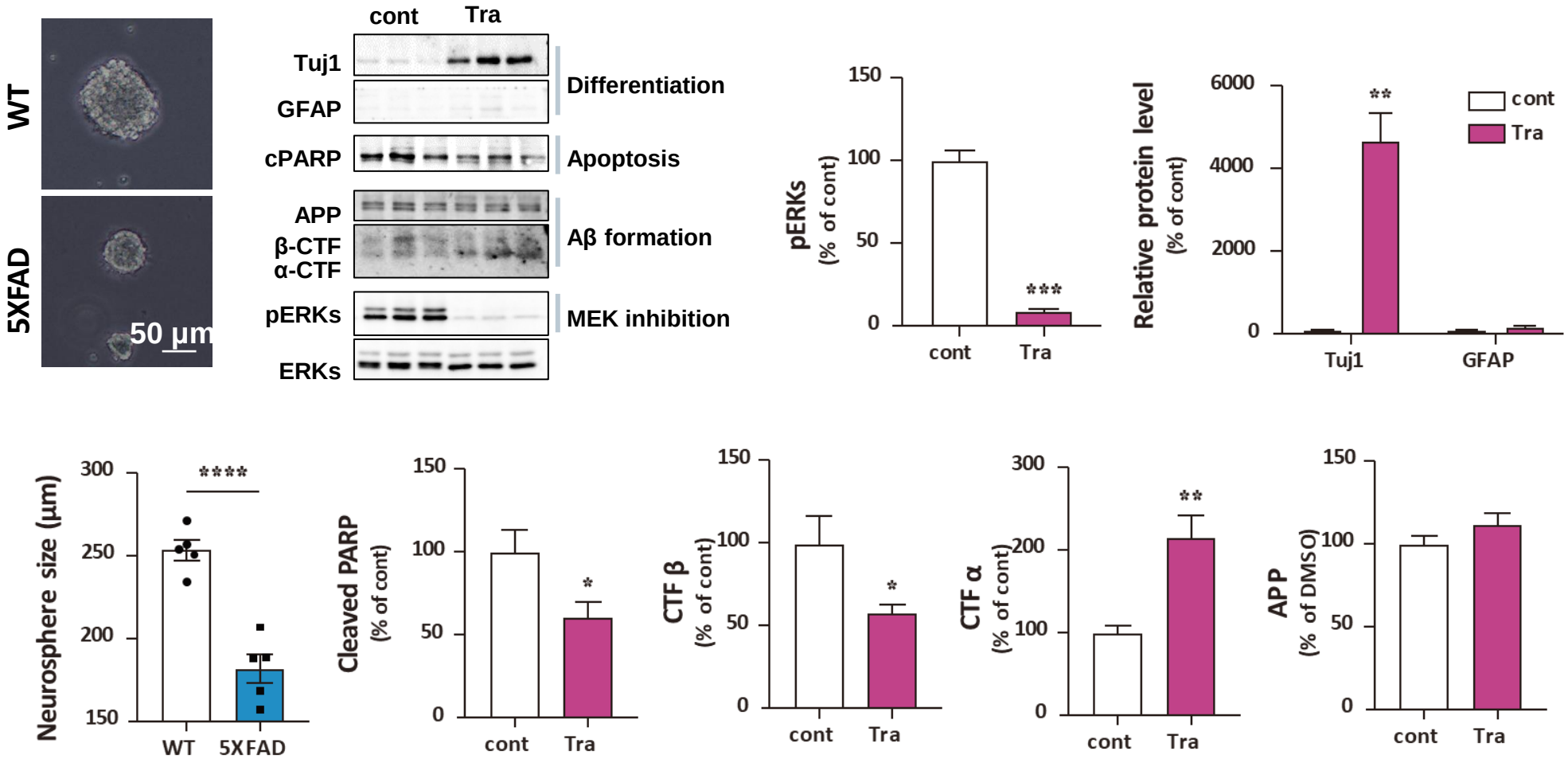


Neuronal differentiation & protection effect by trametinib

- SNR1611 (Trametinib, Mekinist®) -

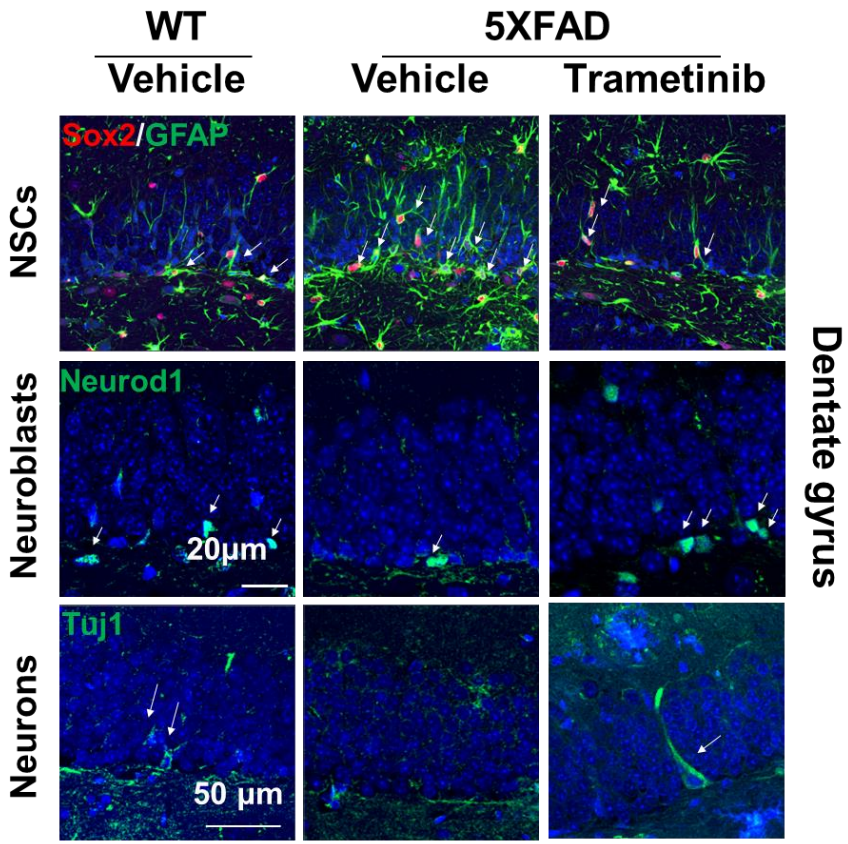
NO – PHOTO / RECORD

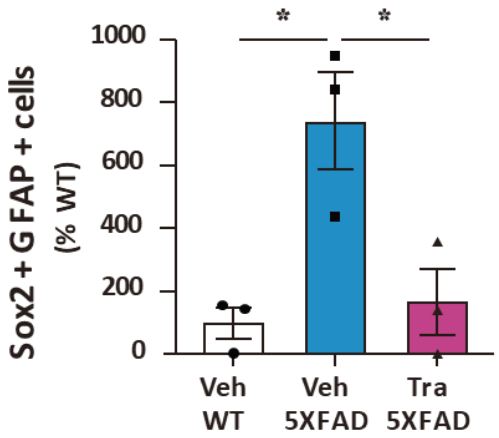
- Inducing Neuronal differentiation & protection of apoptosis in 5XFAD-NSCs by trametinib

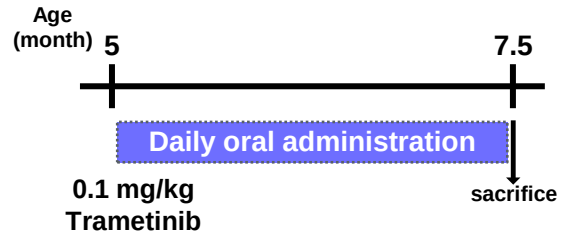


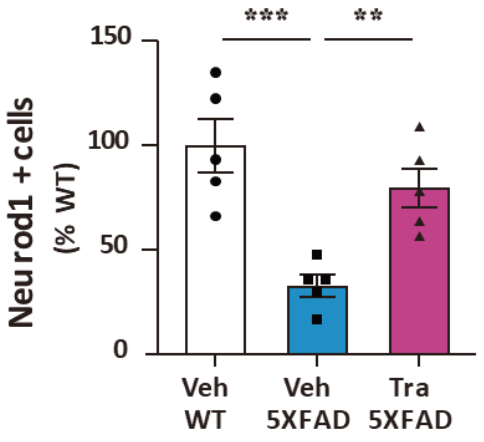
Hippocampal neurogenesis by trametinib in 5XFAD mice

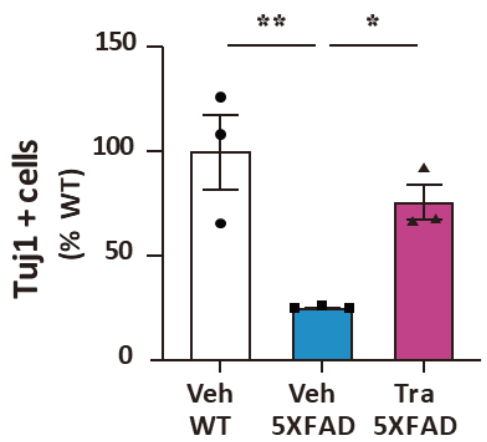
- Trametinib induces hippocampal neurogenesis in 5XFAD mice





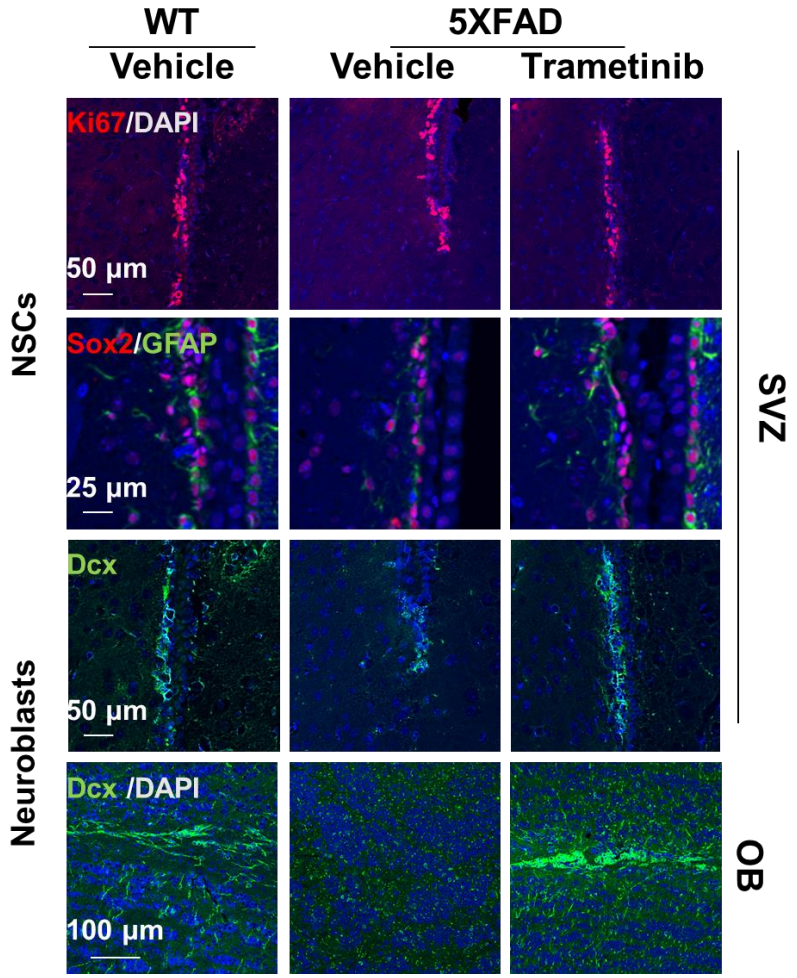


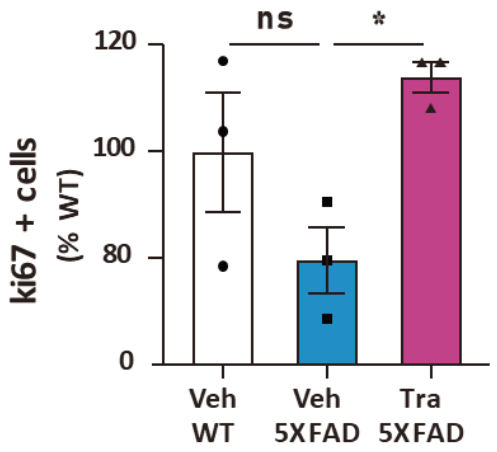


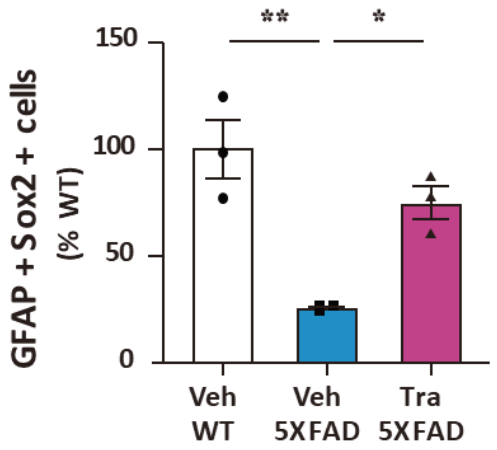


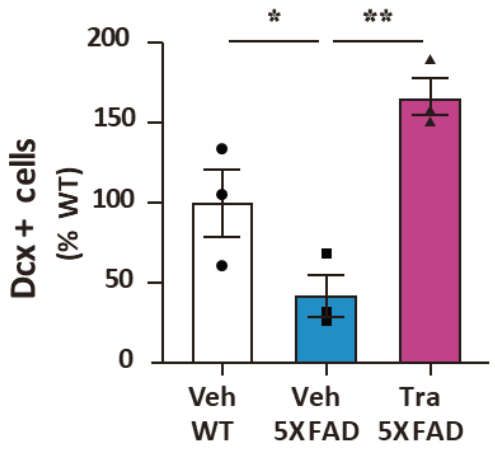
SVZ neurogenesis by trametinib in 5XFAD mice

- Induction of Subventricular zone neurogenesis in 5XFAD mice





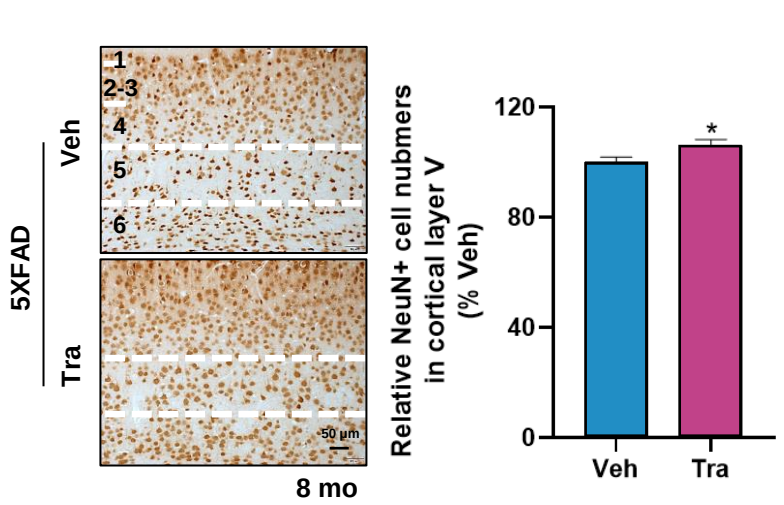


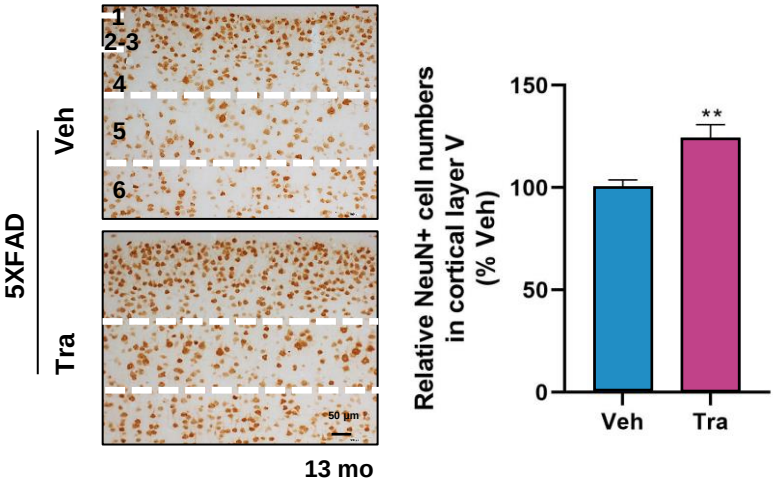


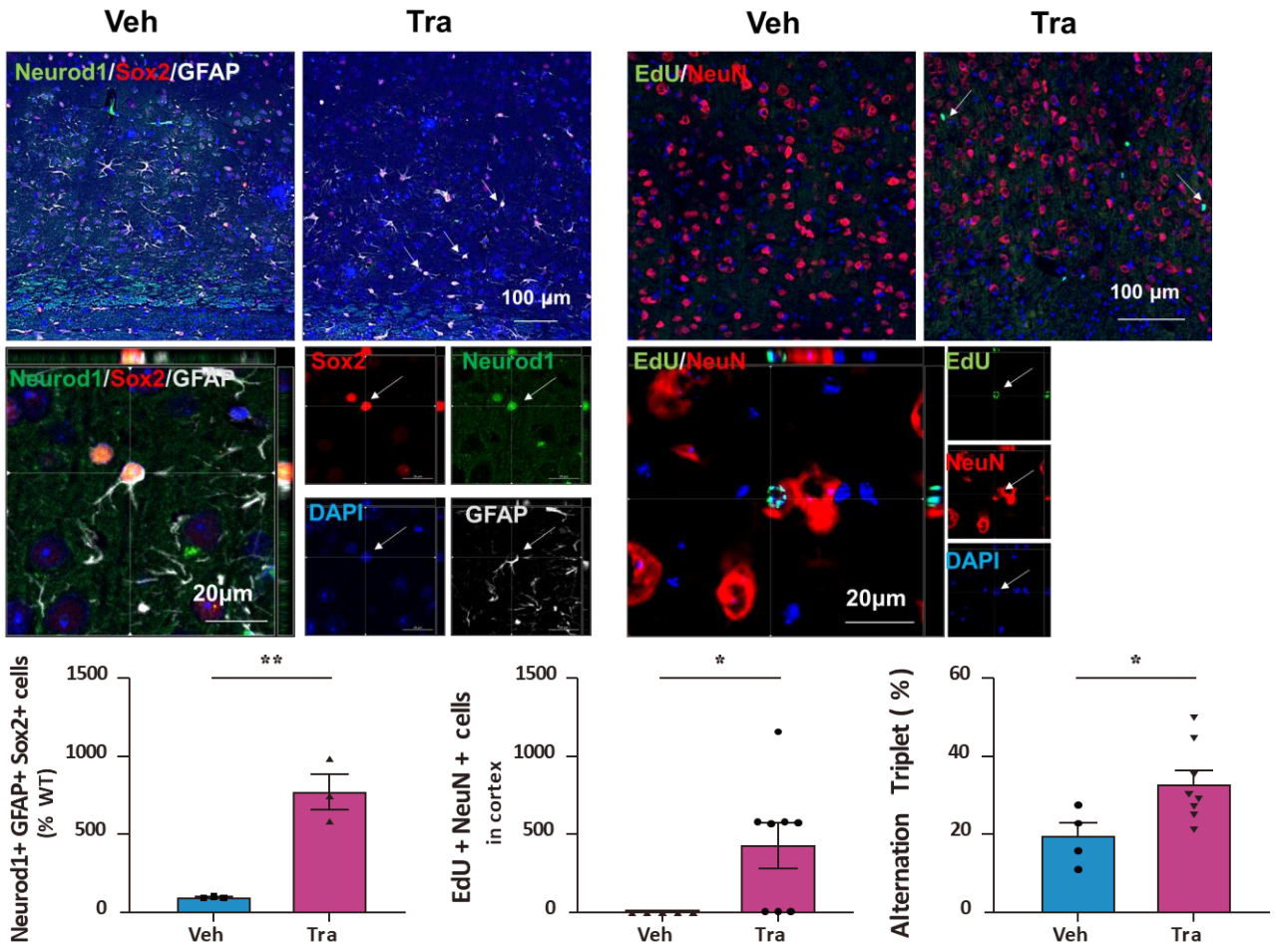
Cortical neurogenesis & Cognitive function by trametinib

NO – PHOTO / RECORD

- Induction of Cortical neurogenesis & rescue of cognitive function in 5XFAD mice

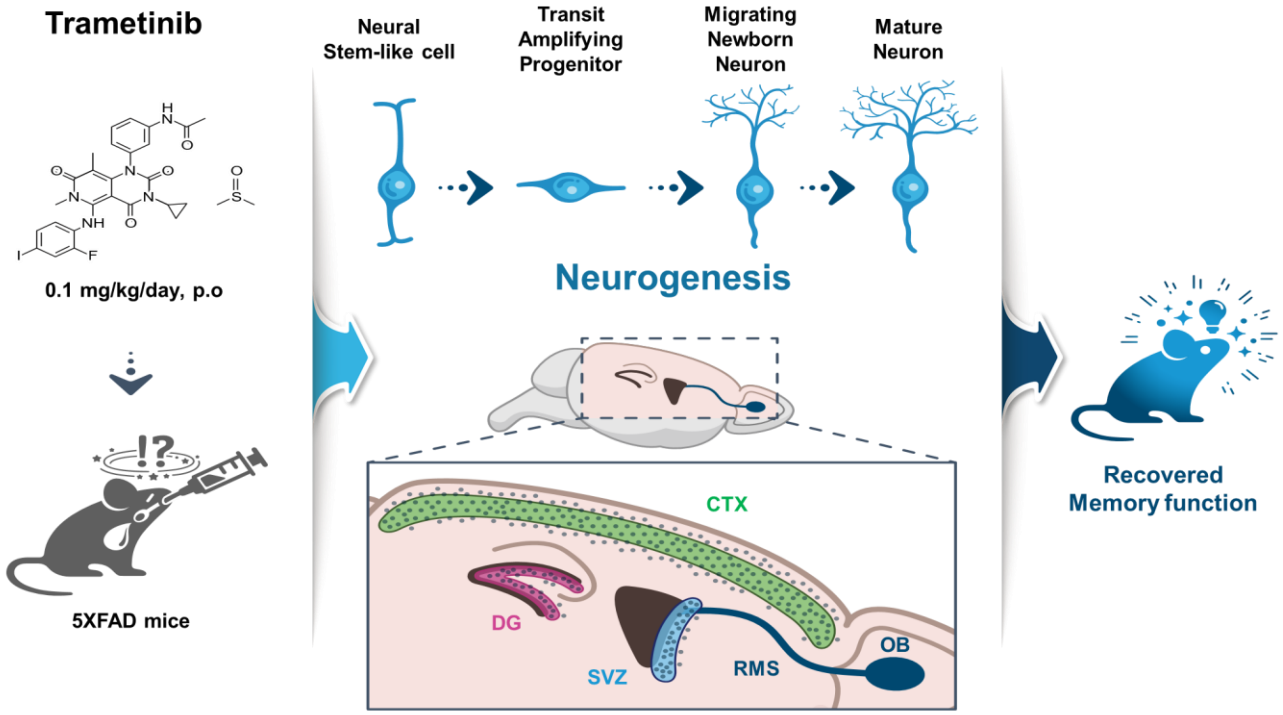






Conclusion

Neurogenesis by Trametinib recovers cognitive function on AD model mouse



1. We established a regenerative drug screening platform, ATRIVIEW®, using NSCs derived from AD-model mice
2. SNR1611 is a very effective drug in enhancing neurogenesis
3. Oral administration of SNR1611 (trametinib) restored impaired neurogenesis in the DG & SVZ of 5XFAD mice
4. We provided evidence that NPCs exist in the brain cortex & SNR1611 induces cortical neurogenesis
5. Restoration of endogenous neurogenesis in the cortex as well as in the DG/SVZ contributes to the recovery from neurodegenerative diseases
6. Enhancing neurogenesis might be a novel therapeutic approach for neurogenerative diseases

Acknowledgement

GENUV

Neuroscience Research Center

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Mi Jeong Kim Researcher, BS

KAIST

KAIST

Department of Biological Sciences

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Thank You