

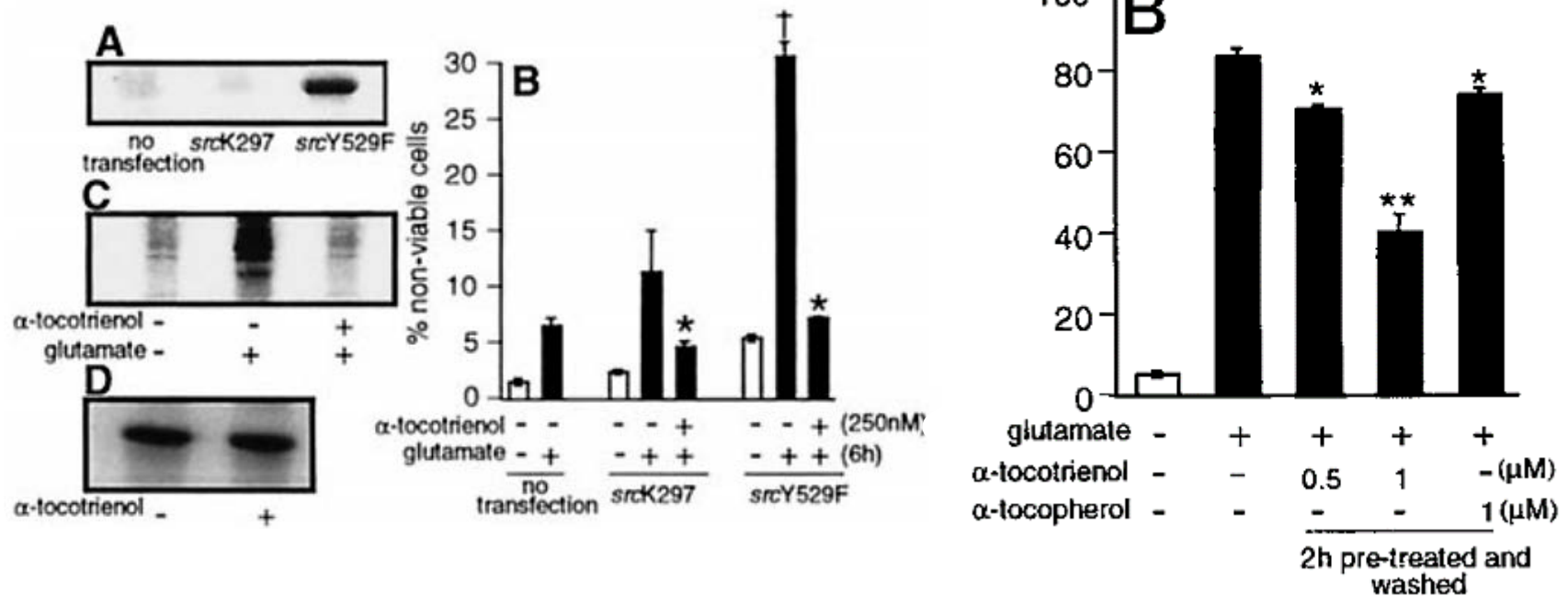


Tocotrienols and their effects on microglia: **implications for brain inflammatory conditions**

Sharmili Vidyadaran



Tocotrienols provide direct neuroprotection



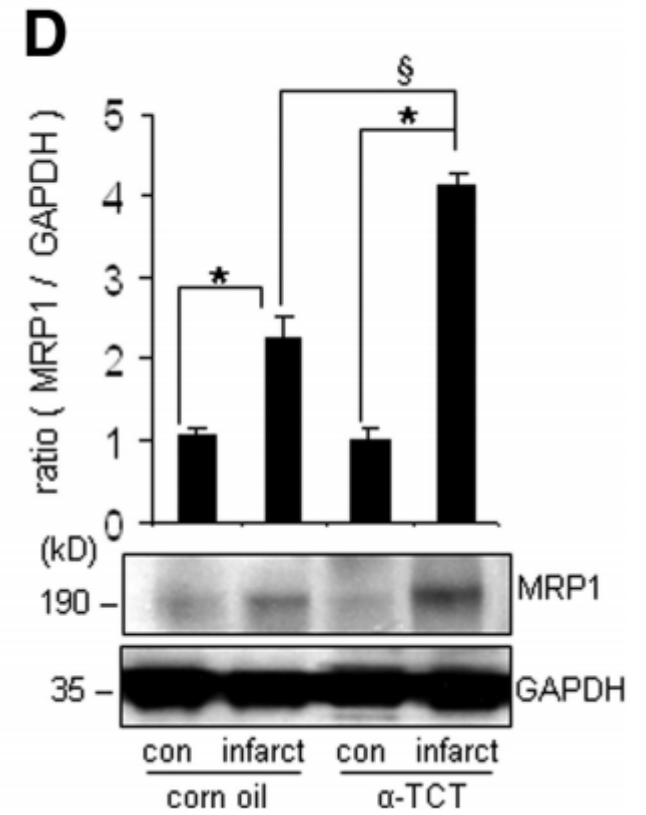
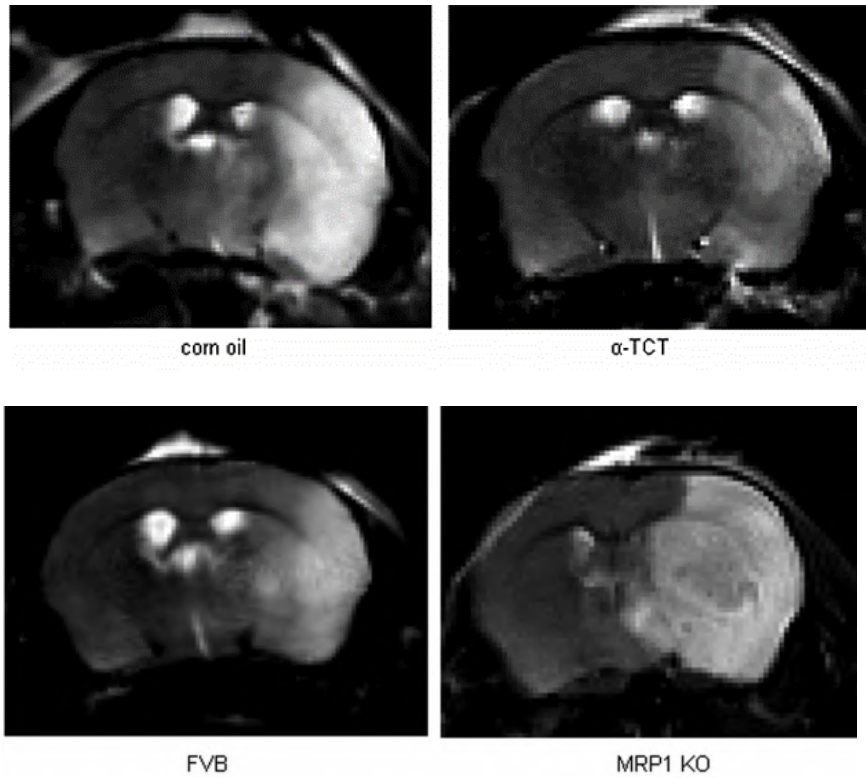


Table 2

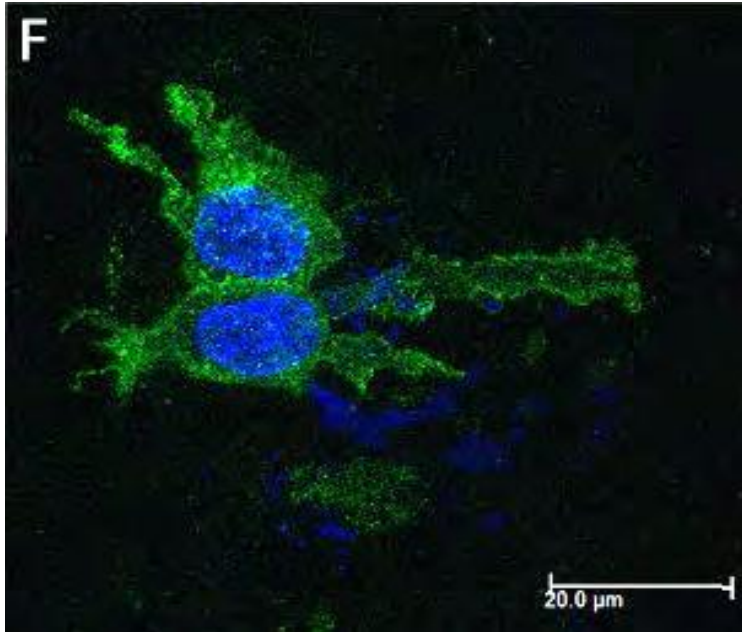
In vitro studies with tocotrienols for effects against cancer, cardiovascular and neurodegenerative diseases.

Neurodegenerative disorders

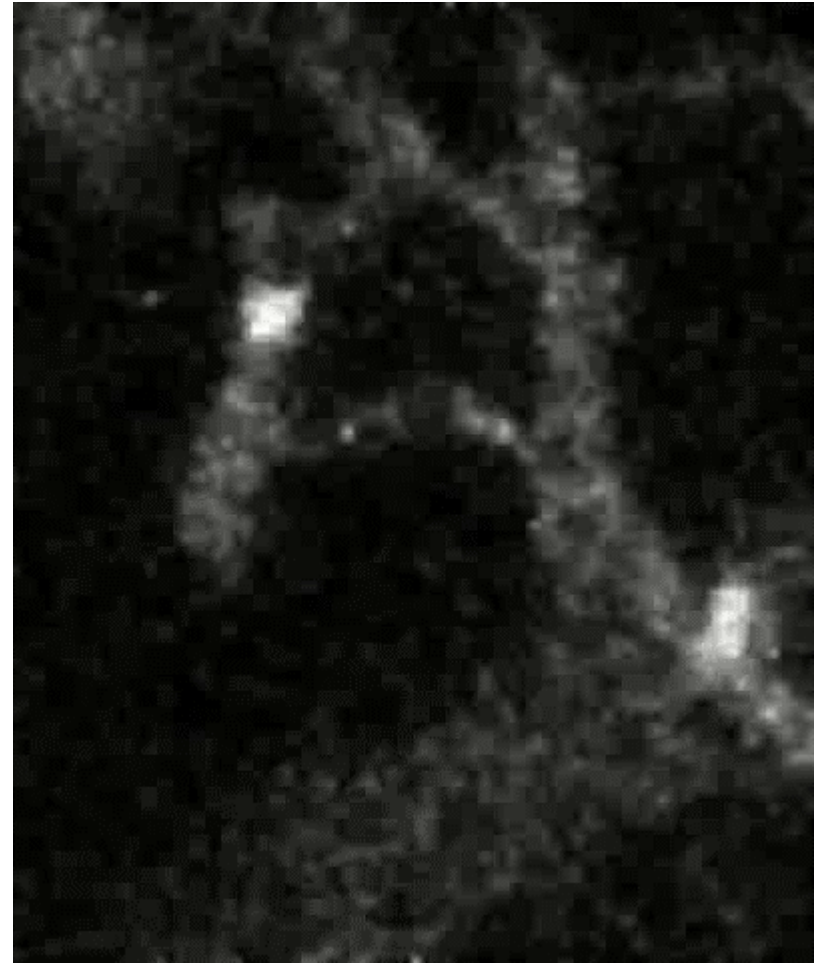
Inhibited glutamate-induced death of HT4 neuronal cells	[55]
Inhibited H ₂ O ₂ -induced neuronal death and oxidative stress-mediated cell death	[217]
Attenuated homocysteic acid-induced neurotoxicity	[92]
Prevents oxidative stress stimulated cell death of cortical neurons cells	[218]
Protected methylmercury-induced neuronal cell death	[188]

Aggarwal *et al.* (2010) *Biochemical Pharmacology*. 1613-1631

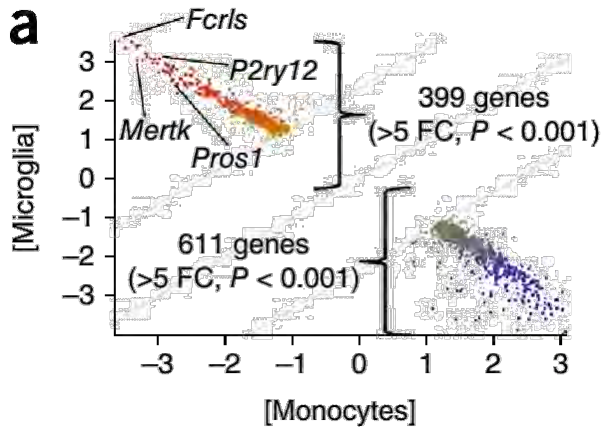
Microglia: CNS macrophages



Haw, Tong, Yew, Lee, Phillips, Vidyadaran. *J Neuroinflammation*. (2014) 11:134.

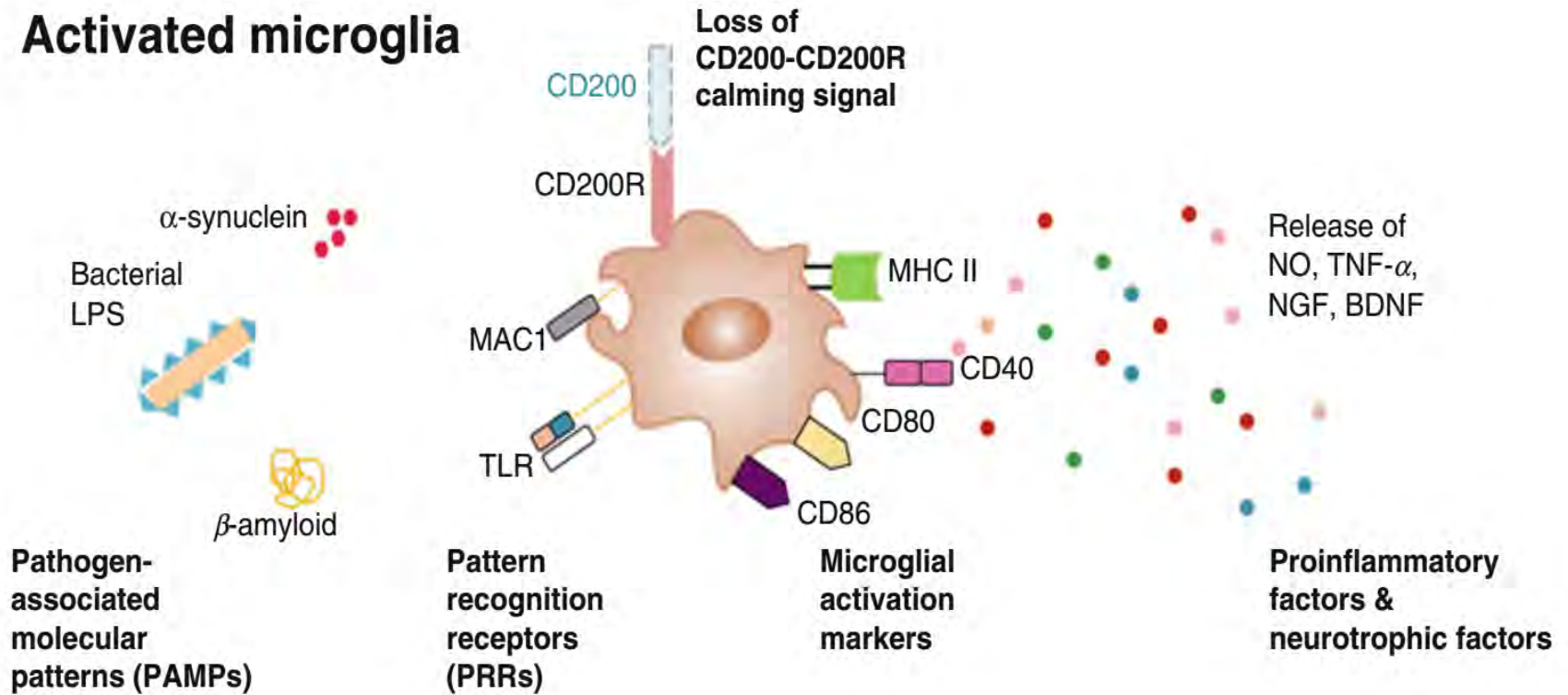


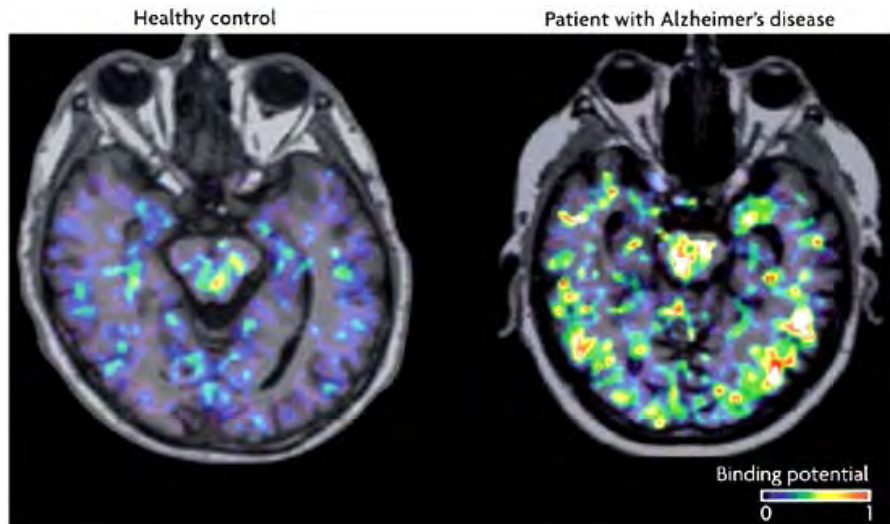
Nimmerjahn *et al. Science*. (2005). 308:1314



Butovsky *et al. Nat Neurosci*. (2014) 17:131-43.

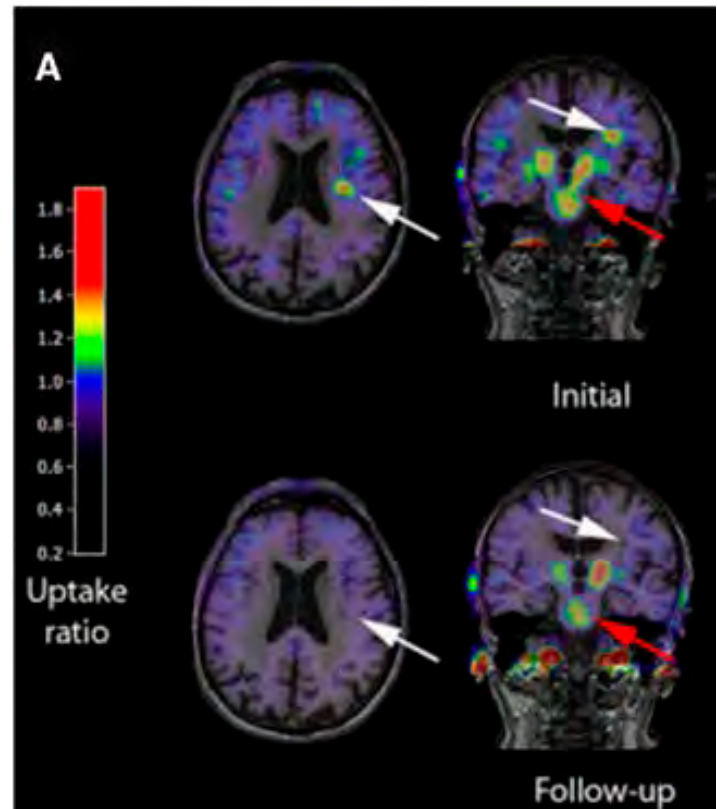
Activated microglia





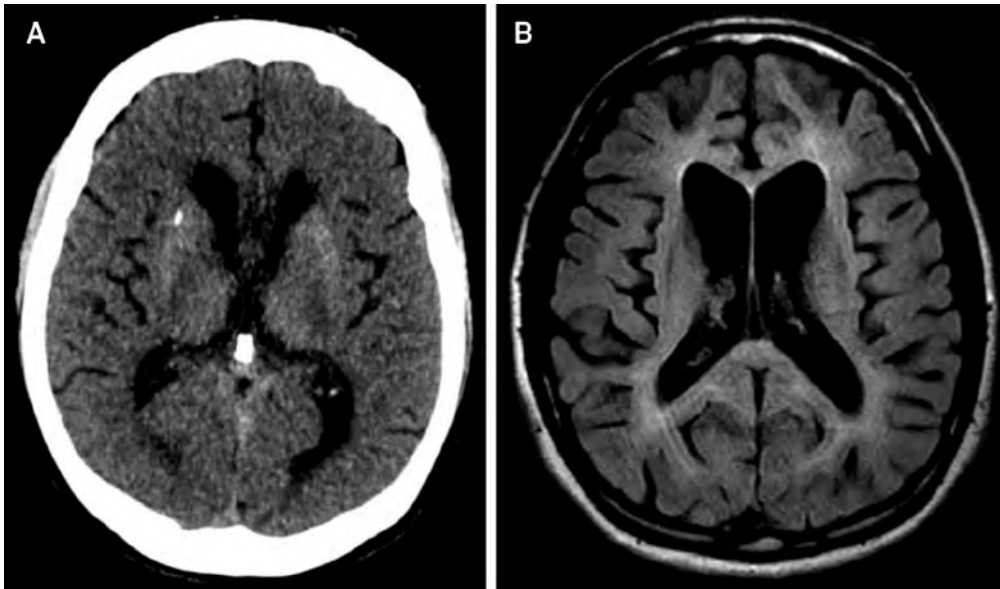
Nature Reviews | Neuroscience

Block, Zecca & Hong (2007) *Nat Rev Neurosci.* 8:57



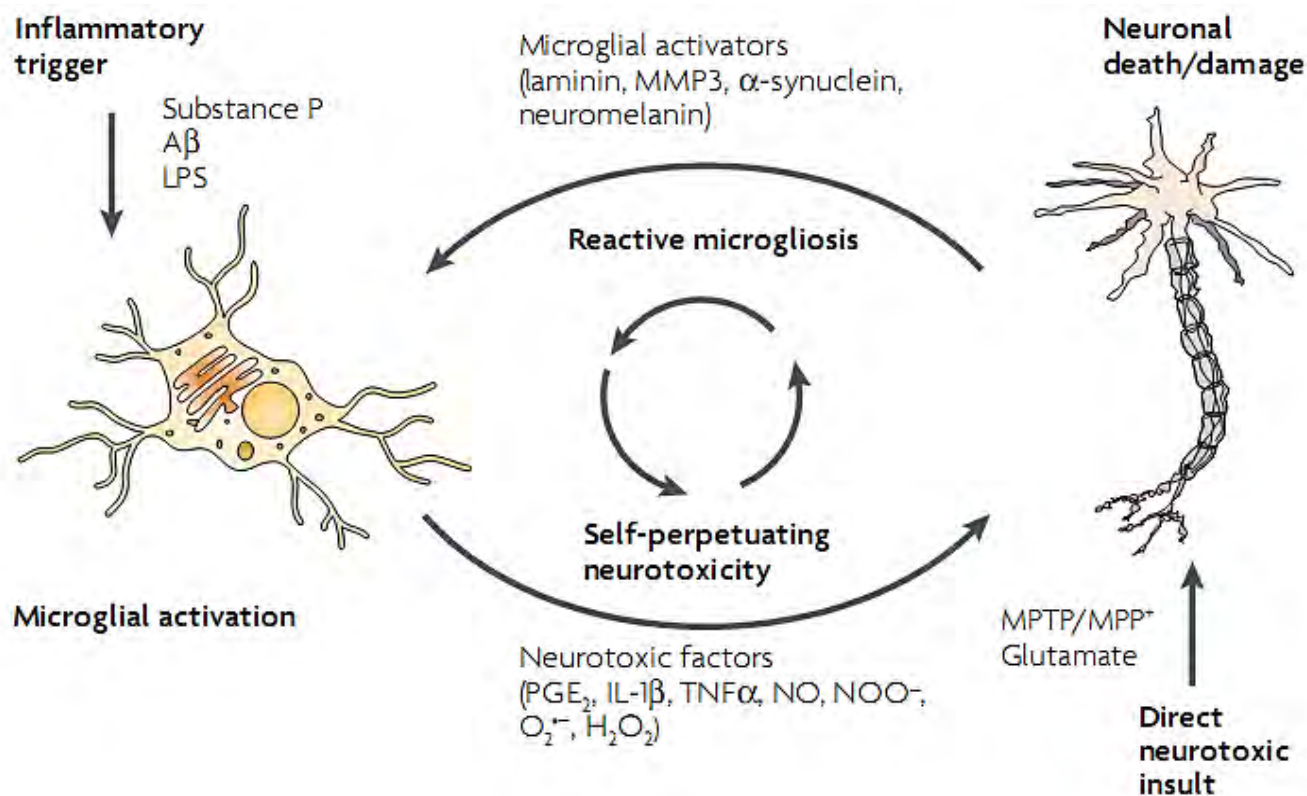
Jacobs, Tavitian & INMiND Consortium (2012)
J Cereb Blood Flow & Metab. 32:1393

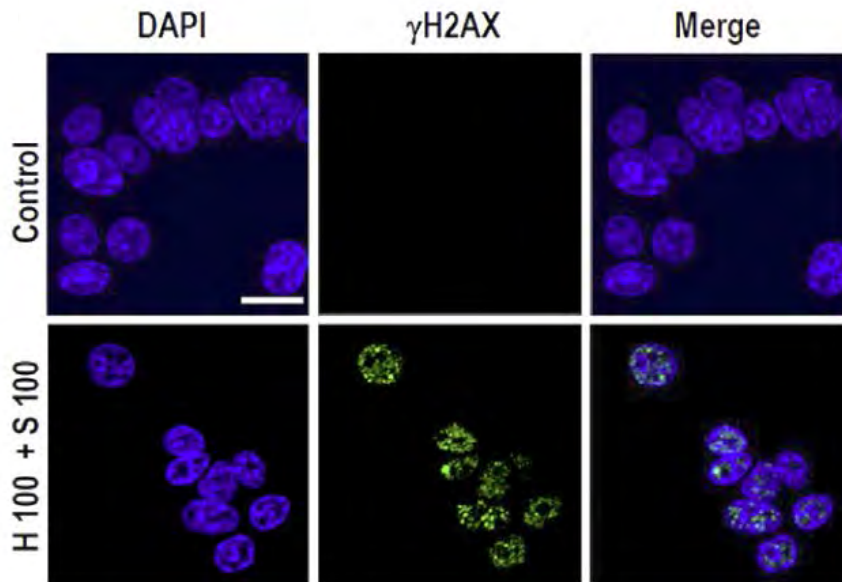
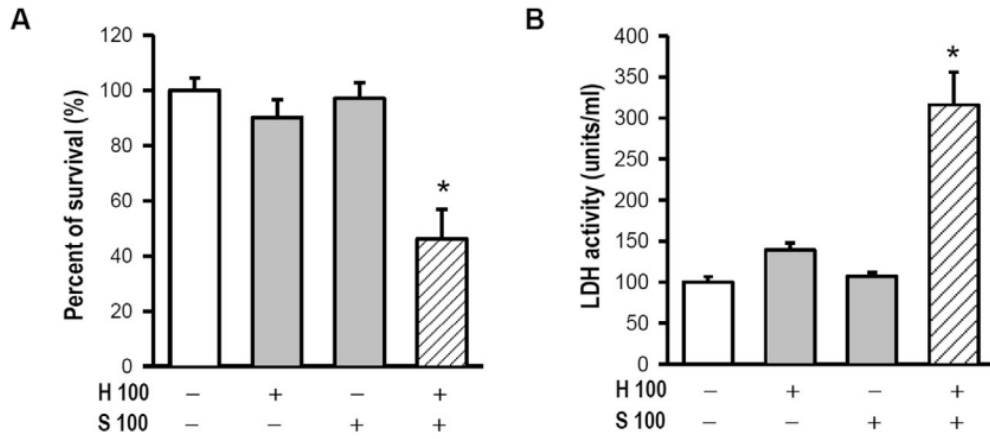
Genetic disorder of microglia function



Nasu-Hakola disease in a 46-year-old man. Unenhanced CT (A) shows punctate calcifications in the lentiform nuclei. Axial FLAIR image (B) demonstrates mild hyperintensity in the periventricular white matter. Note cortical atrophy.

Microglia-induced neurotoxicity





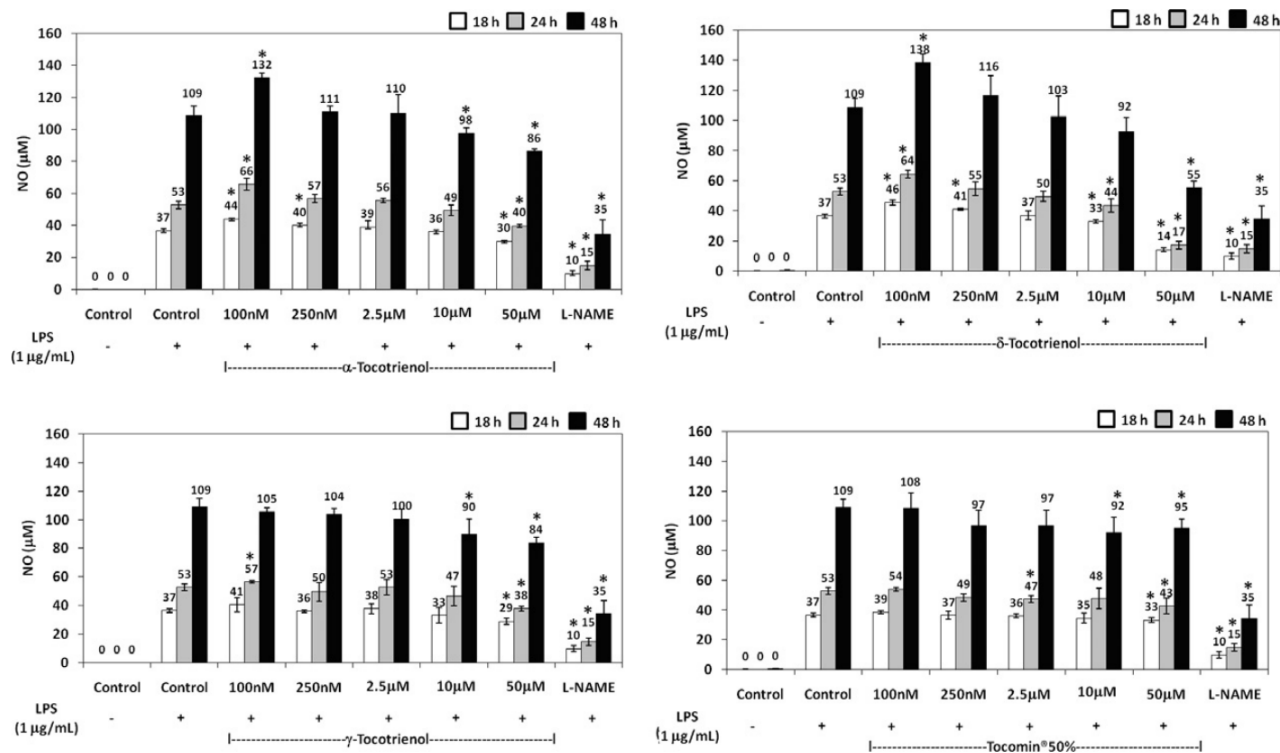


Rapid Communication

Inhibitory effects of palm α -, γ - and δ -tocotrienol on lipopolysaccharide-induced nitric oxide production in BV2 microglia

Shi Wei Tan, Rajesh Ramasamy, Maha Abdullah, Sharmili Vidyadaran*

Immunology Laboratory, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Malaysia





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Biochemical and Biophysical Research Communications 319 (2004) 1047–1052

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Anti-inflammatory effects of tocopherol metabolites

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Journal of Neuroimmunology 149 (2004) 101–109

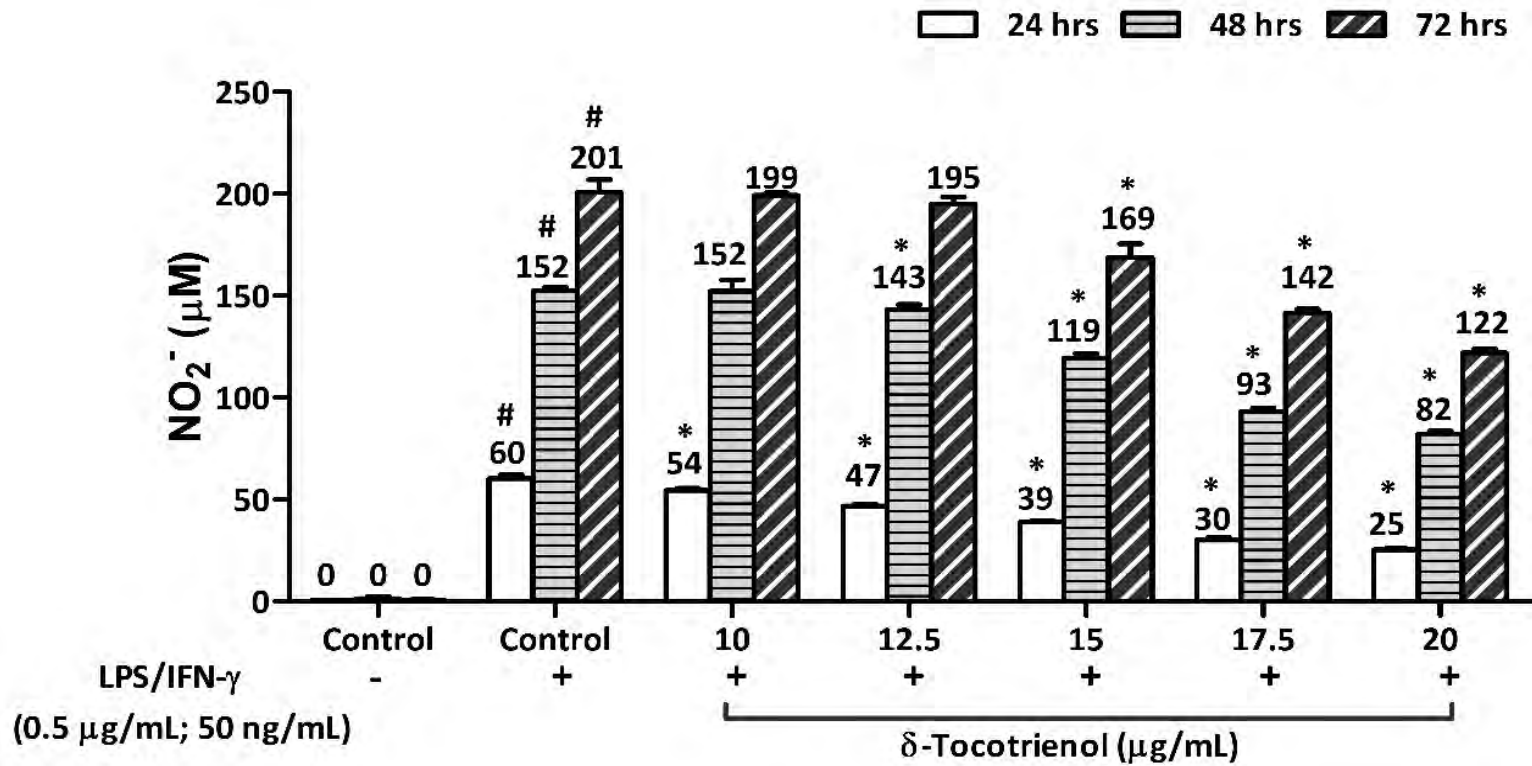
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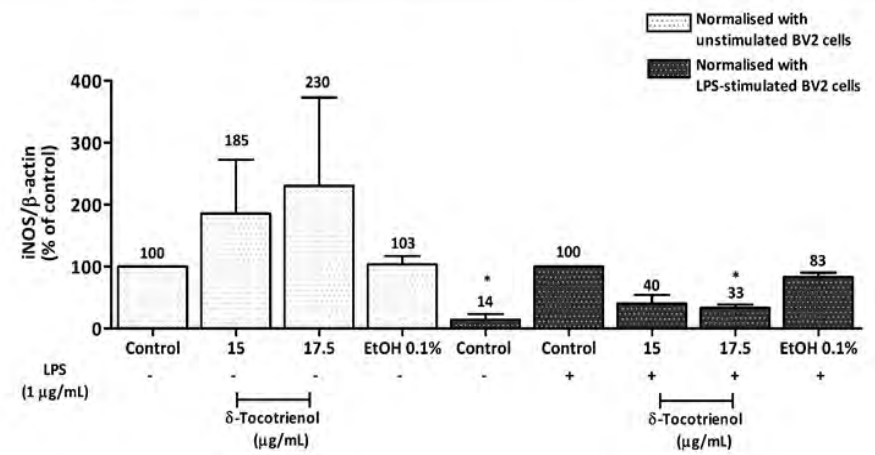
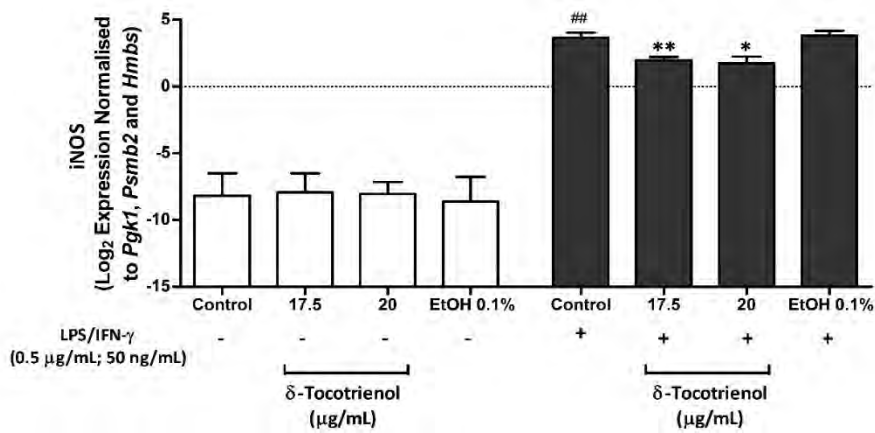
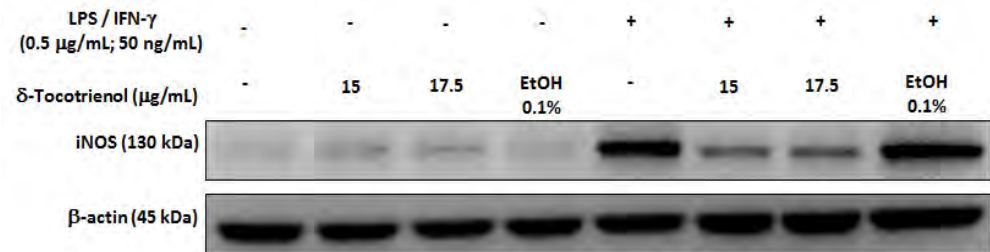
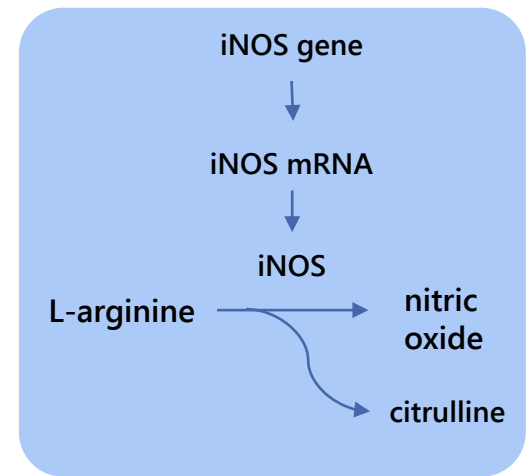
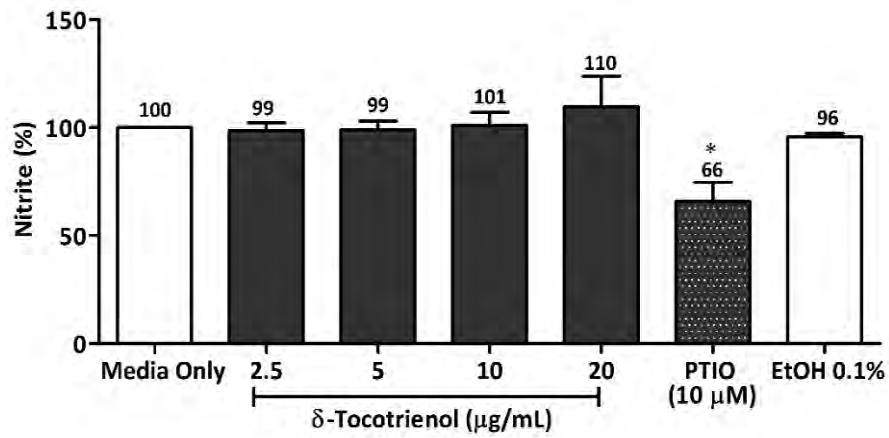
α -Tocopherol reduces lipopolysaccharide-induced peroxide radical formation and interleukin-6 secretion in primary murine microglia and in brain

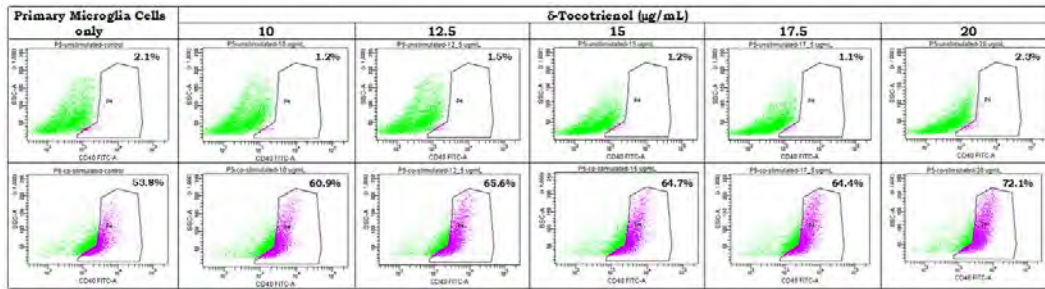
Jonathan P. Godbout, Brian M. Berg, Keith W. Kelley, Rodney W. Johnson*

Department of Animal Sciences and Division of Nutritional Sciences, University of Illinois at Urbana-Champaign, Urbana, IL 61801, USA



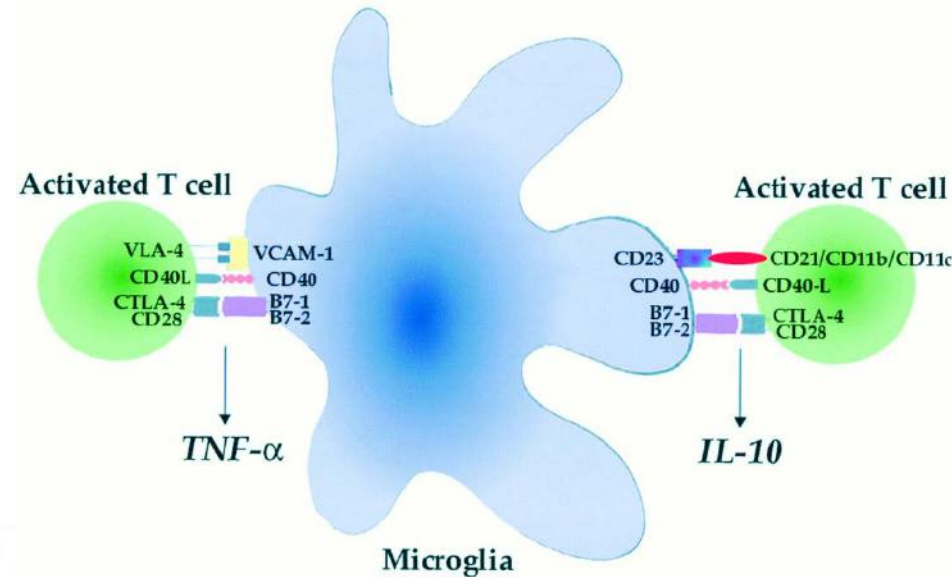
δ-tocotrienol inhibits NO production of primary microglia.



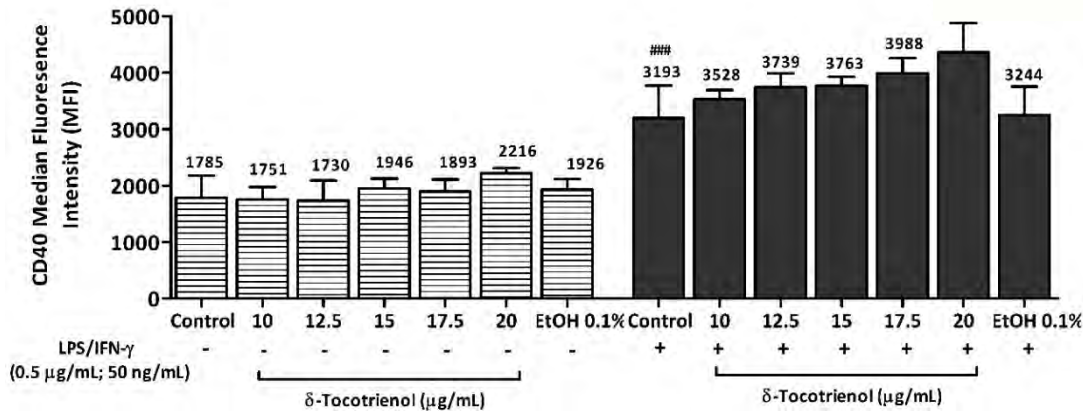


d-T3 (μg/ml)	% CD40+ microglia	
	Unstimulated	LPS-stimulated
0	2.1	53.8
10	1.2	60.9
12.5	1.5	65.6
15	1.2	64.7
17.5	1.1	64.4
20	2.3	72.1

MICROGLIA-T CELL INTERACTION



Chabot *et al. J Immunol* 1999;162:6819-6828



Tan & Vidyadaran, unpublished data



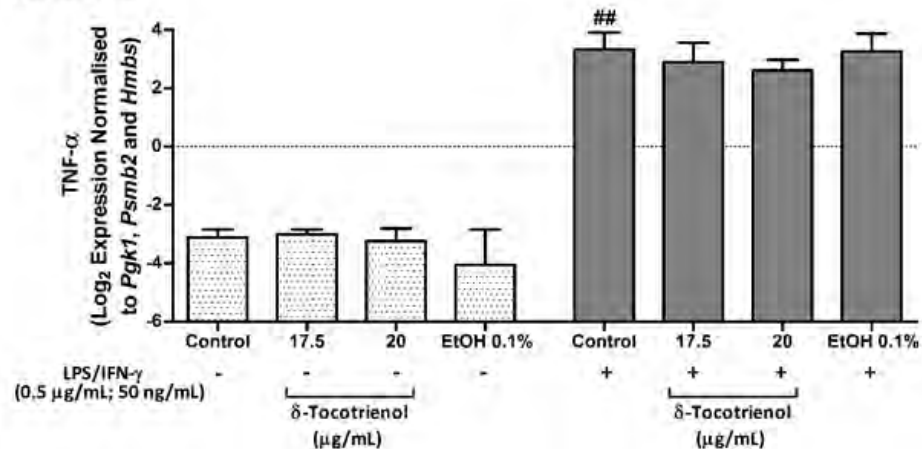
RESEARCH

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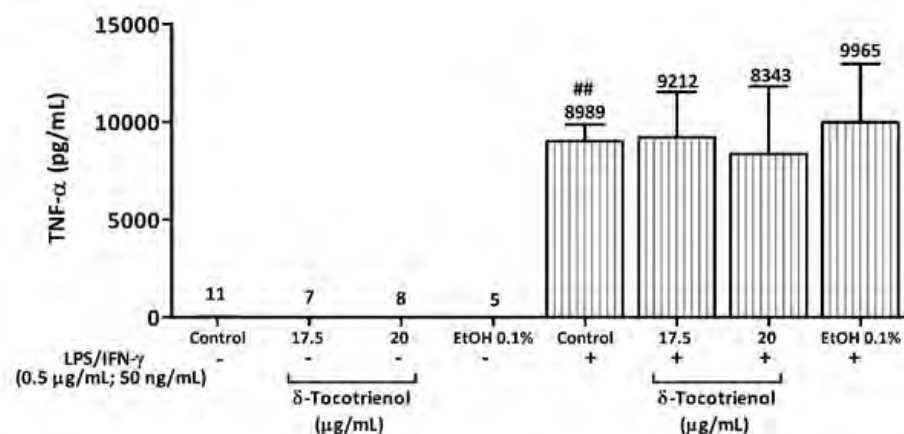
Mesenchymal stem cells exert anti-proliferative effect on lipopolysaccharide-stimulated BV2 microglia by reducing tumour necrosis factor- α levels

Shinsmon Jose^{1,2,3}, Shi Wei Tan¹, Yin Yin Ooi⁴, Rajesh Ramasamy^{2,5} and Sharmili Vidyadaran^{1,2*}

(A) mRNA

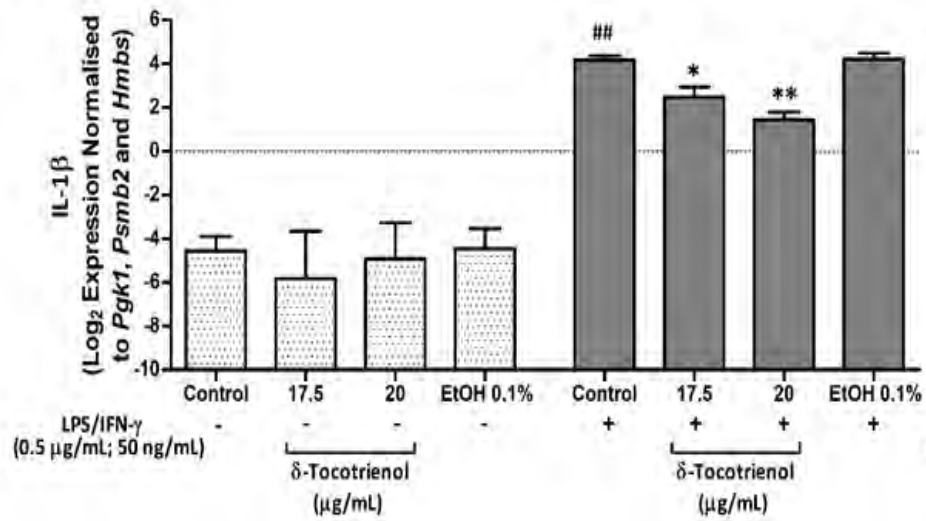


(B) Protein

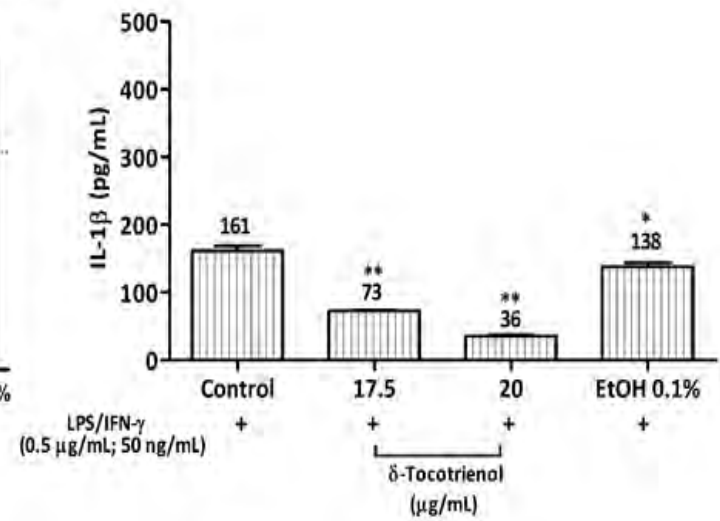




(A) mRNA

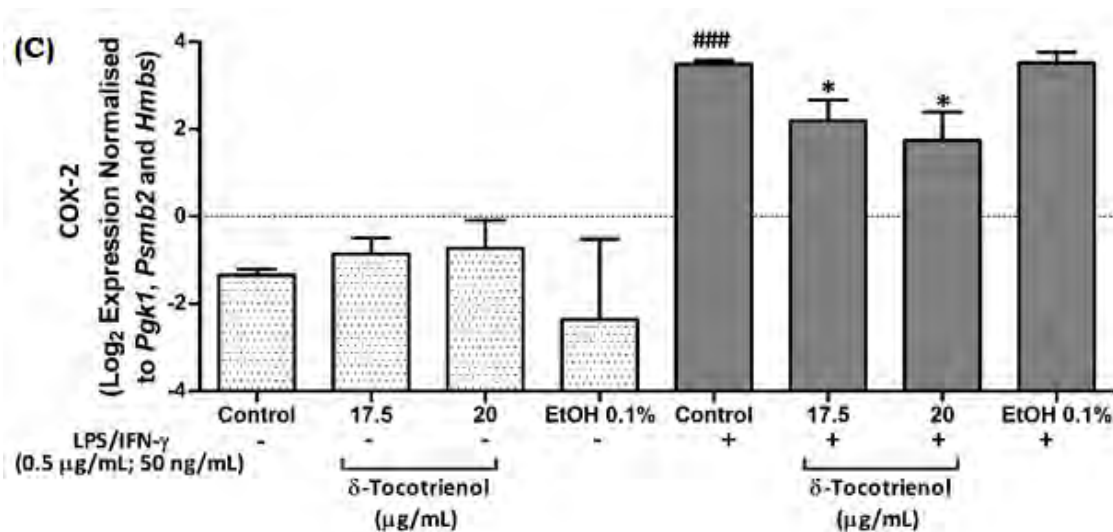
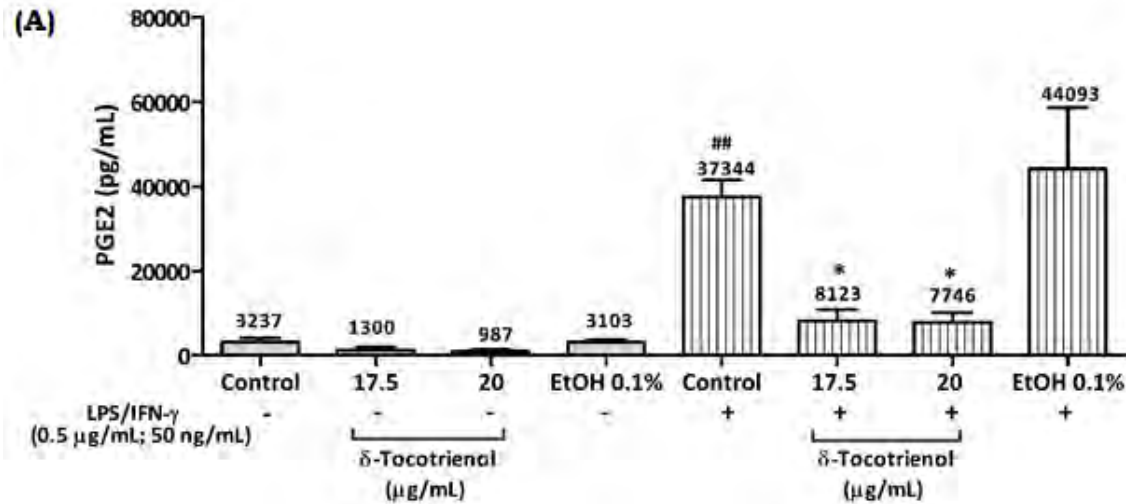


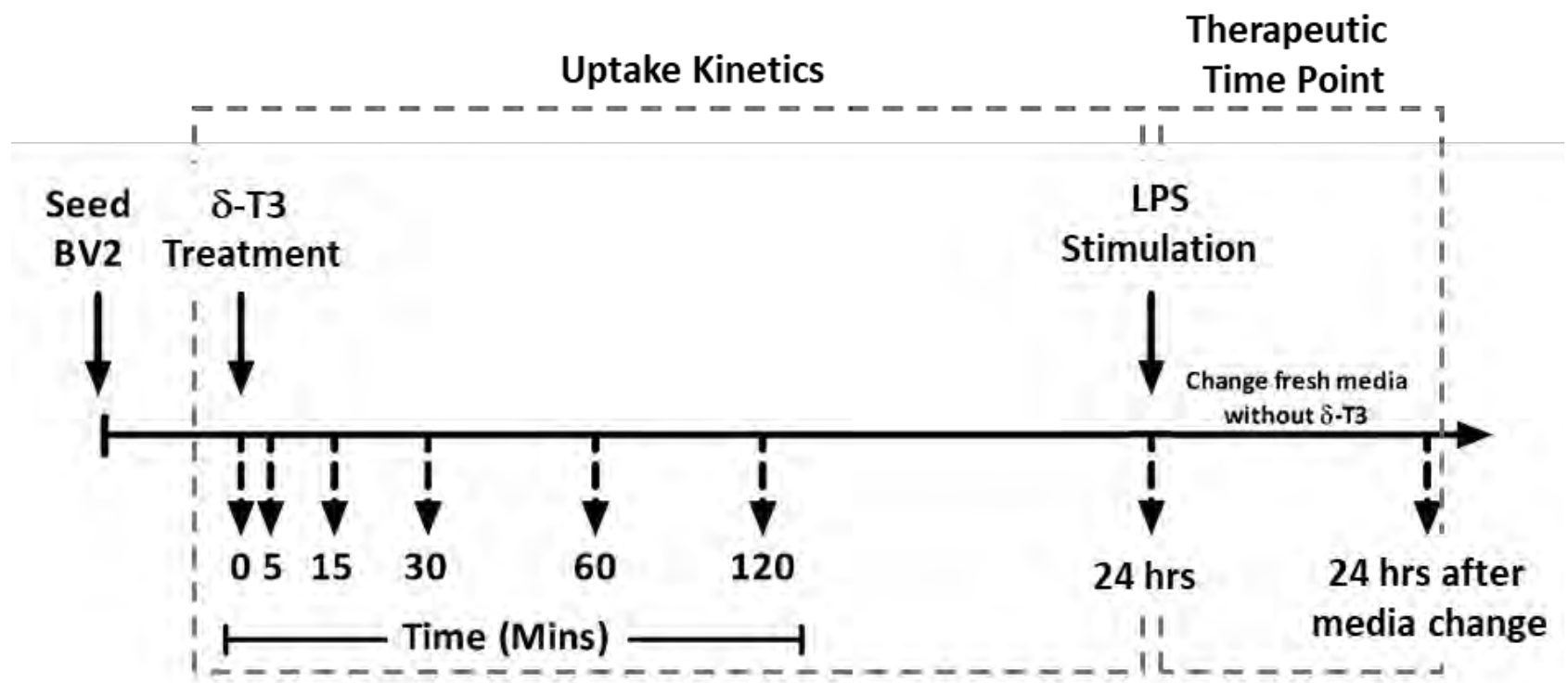
(B) Protein

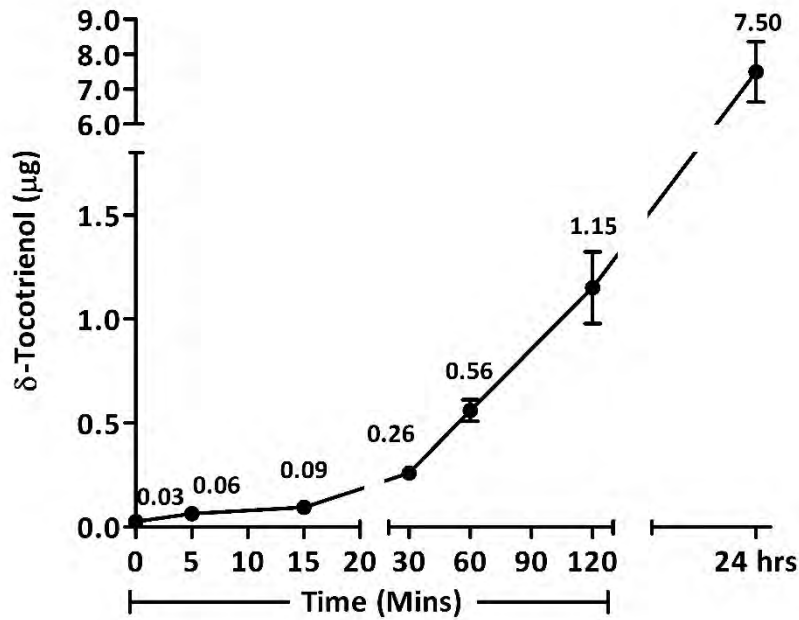


Tan & Vidyadaran, unpublished data

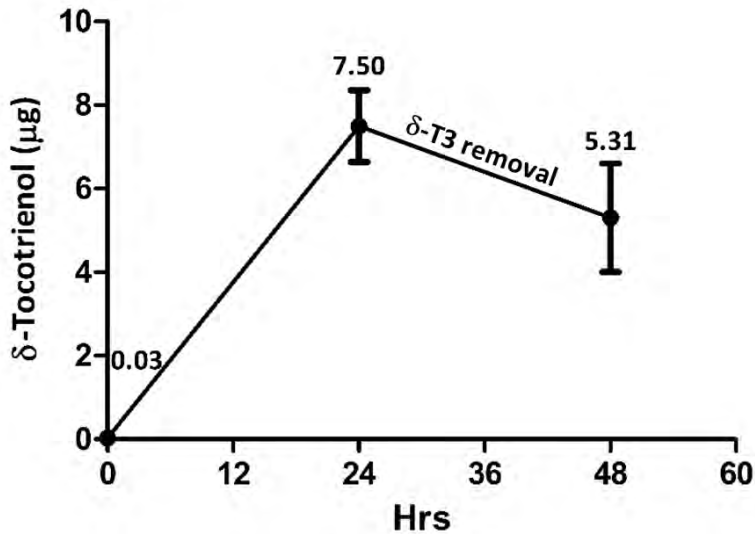
δ -tocotrienol inhibits PGE₂ production of primary microglia, which appears dependent on COX-2.



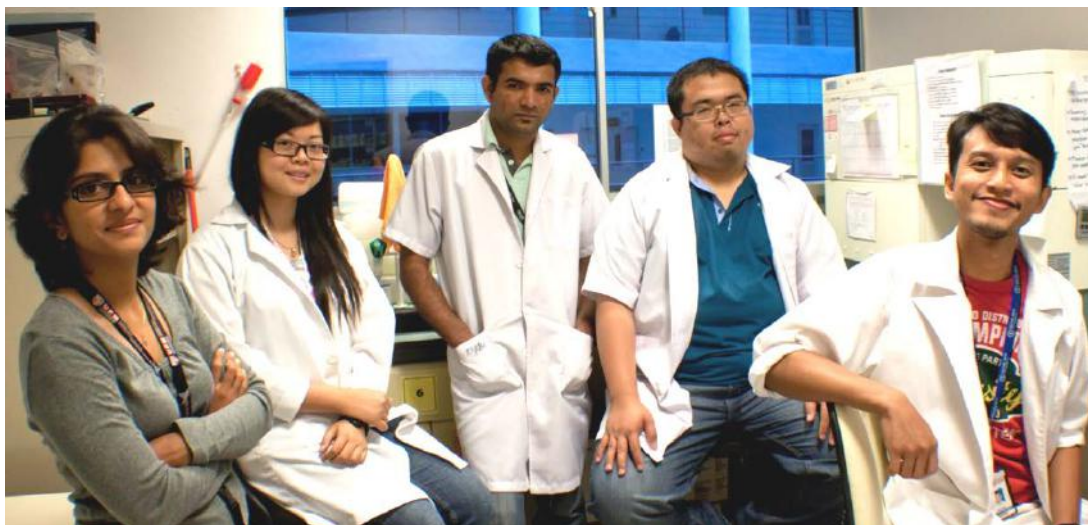




Uptake kinetics of δ -tocotrienol in BV2 microglia cells in 24 hrs.



Retention of δ -tocotrienol in BV2 microglia following removal of δ -tocotrienol.



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THIRD ANNOUNCEMENT

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