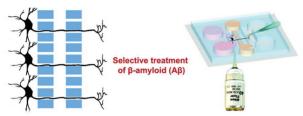
## ACS Chemical Neuroscience

## MICROFLUIDIC PLATFORM FOR EXPLORING AXONAL TRANSPORT



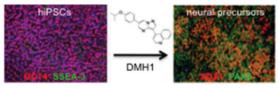
Compartmentalized culture

Compartmentalized measurement

Axonal transport plays a critical role in the transmission of signals in neurons. More recently, a link between dysfunctional axonal transport and neurogenerative diseases such as Alzheimer's, Parkinson's, and Huntington's diseases have been suspected. In this issue, Kim et al. (DOI: 10.1021/cn3000026) provide a microfluidic platform for investigating the role of  $\beta$ -amyloid (A $\beta$ ) in affecting mitochondrial transport in full-length axons.

 $A\beta$  has been shown as a major component in forming neuritic plaques in the brain of patients suffering from Alzheimer's disease. Several studies have pointed to a link between  $A\beta$  toxicity and dysfunctional mitochondrial trafficking in the axon. However, the lack of an appropriate approach to assay mitochondrial trafficking has impeded clarifying this link. The authors developed a microfluidic platform to study the effects of  $A\beta$  on mitochondrial transport and observed significant decreases in mitochondrial movement in the vicinity of  $A\beta$ -exposed axonal compartments.

## ■ SMALL MOLECULE PROMOTES NEUROGENESIS



Human-induced pluripotent stem cells (hiPSCs) can be differentiated into cell types from all three germ layers, including several types of nerve cells. New methodologies have provided a platform for researchers to identify underlying causes of neurological diseases. Recent studies have shown that inhibition of the bone-morphogenic protein (BMP) and TGF- $\beta$ 1 pathways, belonging to the transforming growth factor- $\beta$  (TGF- $\beta$ ) superfamily of proteins, results in efficient conversion of hiPSCs to neural precursor cells. In this issue, Neely et al. (DOI: 10.1021/cn300029t) provide a selective small molecule for efficient neurogenesis of hiPSCs.

Previous work has shown that combined inhibition of BMP and TGF- $\beta$ 1 pathways using small molecules, Noggin and SB431542, result in efficient neurogenesis. The authors compare the efficiency of Noggin with another small molecule, DMH-1, to modulate the BMP signaling pathway. The results showed that DMH1 can replace Noggin for efficient neurogenesis when used in combination with SB431542.

## LYSINE RESIDUES CRITICAL TO $\beta$ -AMYLOID TOXICITY



K28: Major impact on AB assembly

The aggregation of amyloid  $\beta$ -protein (A $\beta$ ) into neurotoxic oligomers is an underlying pathological process linked to Alzheimer's disease. Previous work suggests that hydrophobic and electrostatic interactions are involved in A $\beta$  aggregation and oligomerization. In the current issue, Sinha et al. (DOI: 10.1021/cn3000247) identify two key lysine residues involved in A $\beta$  assembly.

By substituting alanine at lysine-16 and lysine-28 in the  $A\beta$ 40 and  $A\beta$ 42 sequences, the authors demonstrated the critical role of these residues in assembly and toxicity. These important findings suggest that lysine-16 and lysine-28 are good targets for  $A\beta$  assembly inhibitors and modulators.