

**Sebastian Lewandowski - Bio**

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**Abstract**. Although the core symptoms of ALS feature rapid, degeneration of motor neurons, we still know little how other cells including blood vessels contribute to ALS etiology. Our work shows that cerebral perivascular fibroblast cells become active long before the onset of neuroinflammation and remodel perivascular spaces with specific collagen and chemokine proteins in ALS mouse models and sporadic ALS patients (Månberg et al. *Nature Medicine* 2021). Targeted plasma proteomics of 452 ALS patients showed that perivascular fibroblast specific proteins increase vastly outperforms current standards of prediction for patient survival. We believe our results provide a novel conceptual framework to re-evaluate cellular contributions to etiology and dynamics of ALS neurodegeneration. Since enlarged perivascular spaces are repeatedly observed in aging, dementia and other neurological disorders, perivascular fibroblast cell activity could represent a common mechanism in cerebral injury response.

**Biosketch**

- Dr Lewandowski’s research aims to explain the interdependence between the neuronal and vascular cells. His recent work has shown that brain vascular fibroblasts are activated before the onset of neuroinflammation and neurodegeneration in ALS (Månberg et al 2021). His future studies in ALS could help to redefine the mechanisms of ALS etiology, clinical prognosis and therapy.

- Dr Lewandowski is a member of the Swedish Medical Association, Swedish Society for Neuroscience and a steering group member of the junior faculty at the Karolinska Institute. He has received grants for his ALS research from the Ulla-Carin Lindquist Foundation, the Åhlens Foundation, and the Olle Engkvist Byggmästare Foundation.

- He received his undergraduate degree from the University of Gdansk and obtained his PhD in molecular biology from the Nencki Institute of Experimental Biology in Warsaw. He performed his postdoctoral training at laboratory of Prof. Ulf Eriksson at the Karolinska Institute.

**Selected publication list
1.** *Altered perivascular fibroblast activity precedes ALS disease onset.* Månberg A, (…) **Lewandowski SA**. Nature Medicine. 27:640–646 (2021) PMID: 33859435

**2***. Presymptomatic activation of the PDGF-CC pathway accelerates onset of ALS neurodegeneration*. **Lewandowski SA** et al. Acta Neuropathologica 131:453-64. (2016) PMID: 26687981,

**3.** *Pharmacological targeting of the PDGF-CC signaling pathway for blood-brain barrier restoration in neurological disorders*. **Lewandowski SA** et al. Pharmacology & Therapeutics. 167:108–119. (2016) PMID: 27524729,

**4.** *Vascular regression precedes motor neuron loss in the FUS (1-359) ALS mouse model.* Crivello M, et al. Disease Model Mech. Aug 13;12(8). (2019) PMID:31383794

**5.** *Pleiotropic activity of systemically delivered angiogenin in the SOD1G93A mouse model*. Crivello M et al. Neuropharmacology**.** 133:503-511. (2018), PMID: 29486168