

1. Titre du résumé

Brain glucose metabolism as a readout of the CNS impact of cigarette smoke exposure, withdrawal, and the effects of NFL-101, as an immune-based drug candidate for smoking cessation therapy

2. Coordonnées des co-auteurs

S. Goutal¹, T. Tran^{2,3}, C. Leroy¹, N. Benhamouda^{2,3}, S. Leterrier¹, W. Saba¹, B. Lafont⁴, E. Tartour^{2,3}, M. Roelens^{2,3}, N. Tournier¹

1. CEA, CNRS, Inserm, BioMaps, Université Paris-Saclay, Orsay, France

2. Université Paris Cité, INSERM, PARCC, Paris, France.

3 Department of Immunology, APHP, Hôpital Européen Georges Pompidou (HEGP), Hôpital Necker, Paris, France.

4. NFL Biosciences, Castelnau-le-Lez, France

3. Coordonnées de l'auteur principal qui sera le contact pour le Congrès de l'ALBATROS

Nicolas Tournier (PhD, PharmD)

CEA, CNRS, Inserm, BioMaps, Université Paris-Saclay, Orsay, France

n.tournier@universite-paris-saclay.fr

Résumé

4. Description précise des objectifs

Neuroimaging biomarkers are needed to *i)* better understand the neural mechanisms underlying cigarette-smoking withdrawal, and *ii)* evaluate the efficacy of drug candidates for smoking cessation therapies. NFL-101 is a denicotinized aqueous extract of tobacco leaves, currently investigated as an immune-based smoking cessation therapy in humans. However, the immune response to NFL-101, and its ability to induce significant changes in brain function remain to be demonstrated.

5. Matériel et méthodes

First, changes in the resting-state brain glucose metabolism were investigated using [¹⁸F]fluoro-deoxy-glucose ([¹⁸F]FDG) Positron Emission Tomography (PET) imaging in a mouse model of Cigarette Smoke Exposure (CSE, 4-weeks whole-body inhalation, twice daily), after overnight withdrawal. The immunogenic property of NFL-101 was investigated in some mice using a standardized protocol. Then, mice of both the control and the CSE group participated in a second [¹⁸F]FDG PET acquisition, after 2 days cigarette smoke withdrawal and injection of a single dose of either NFL-101 or saline.

6. Résultats et conclusions

Compared with control animals, the uptake of [¹⁸F]FDG in CSE mice was decreased in the thalamus and brain stem ($p < 0.001$, $n = 14$ per group), and increased in the hippocampus, cortex, cerebellum and olfactory bulb ($p < 0.001$). The ability of NFL-101 to induce a humoral immune response (specific IgG) was verified in mice. In CSE mice, but not in control mice, a single dose of NFL-101 significantly increased [¹⁸F]FDG uptake in the thalamus ($p < 0.001$), thus restoring normal brain glucose metabolism after 2-day withdrawal in this nicotinic receptor-rich region. In tobacco research, [¹⁸F]FDG PET imaging provides a quantitative method to evaluate changes in brain function associated with the withdrawal phase. This method also showed the CNS effects of NFL-101, with translational perspectives for future clinical evaluation in smokers.

7. Liens d'intérêt

B. Lafont is co-founder, chief operating officer and stockholder of NFL Biosciences as well as inventor of patent applications related to NFL-101. The remaining authors declare no competing interests.