CLA and CLNA ameliorate neuroinflammation and cellular oxidation related with western diets

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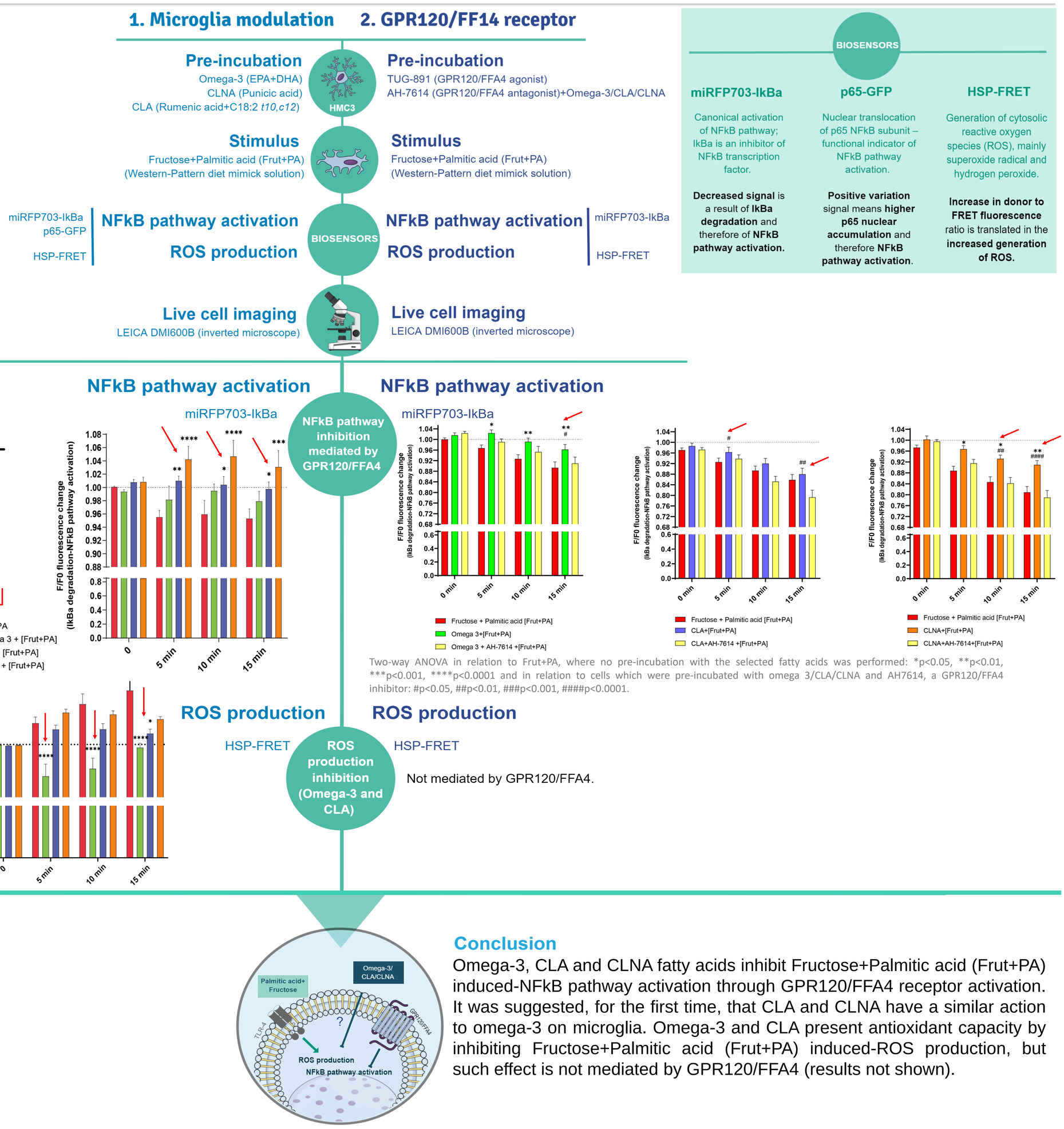
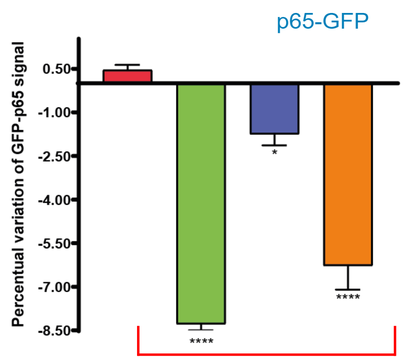
Introduction and objectives

High-fat diet has been associated with a chronic-low grade inflammation in both adipose tissue and central nervous system. Moreover, fatty acids (FAs) are known to cross the blood-brain barrier and reach the central nervous system. Microglia express a wide range of lipid-sensitive receptors, potentially triggering inflammatory responses. Therefore, FAs can exert both pro (*e.g.* saturated fatty acids, SFAs) and anti-inflammatory (*e.g*. polyunsaturated fatty acids, PUFAs) effects in the hypothalamus. Although the mechanisms of action have not been fully described yet, GPR120/FFA4 receptor activation by omega-3 FA results into the inhibition of the NFkB pathway. Considering the beneficial role of conjugated linoleic acid (CLA) and conjugated linolenic acid isomers (CLNA) in obesity, namely their anti-inflammatory properties, we hypothesized that they may present similar properties as omega-3 fatty acids in hypothalamus. Thus, in this work through live cell imaging and FRET technology, and using a human microglia cell model (HMC3), we assessed the modulatory potential of a solution mimicking the western pattern diet (palmitic acid, a SFA, and fructose) and the preventive role of different PUFAs (Omega-3 – EPA and DHA-, CLA and CLNA isomers), specifically targeting the NFkB pathway and oxidative stress through reactive oxygen species (ROS) production. By using chemical agonists (TUG-891) and antagonists (AH-7614) of GPR120/FFA4 we determined if Omega-3, CLA and CLNA modulatory effects are mediated by this receptor.

Experimental design and Results



NFkB pathway activation



Two-way ANOVA in relation to Frut+PA, where no pre-incubation with the selected fatty acids was performed. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

NFkB pathway inhibition mediated by GPR120/FFA4

NFkB pathway activation

Two-way ANOVA in relation to Frut+PA, where no pre-incubation with the selected fatty acids was performed: *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 and in relation to cells which were pre-incubated with omega 3/CLA/CLNA and AH7614, a GPR120/FFA4 inhibitor: #p<0.05, ##p<0.01, ###p<0.001, ####p<0.0001.

ROS production

ROS production inhibition (Omega-3 and CLA)

ROS production

HSP-FRET

HSP-FRET

Not mediated by GPR120/FFA4.

Conclusion

Omega-3, CLA and CLNA fatty acids inhibit Fructose+Palmitic acid (Frut+PA) induced-NFkB pathway activation through GPR120/FFA4 receptor activation. It was suggested, for the first time, that CLA and CLNA have a similar action to omega-3 on microglia. Omega-3 and CLA present antioxidant capacity by inhibiting Fructose+Palmitic acid (Frut+PA) induced-ROS production, but such effect is not mediated by GPR120/FFA4 (results not shown).

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