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The complement C5a receptor C5L2, traditionally known as a non-functional receptor, negatively regulates brain-derived nerve growth factor secretion in LTA-stimulated human pulp fibroblasts

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Given the importance of sensory innervation in tooth vitality, the identification of signals that control nerve regeneration and the cellular events they induce is essential to identify new therapeutic targets. The complement anaphylatoxin C5a, which is one of the very first components of innate immunity and inflammation is produced at the injured site of human carious teeth and plays an important role in dental-pulp regeneration via interaction with nearby dental pulp cells. We extend these observations in dental nerve regeneration research with regard to local production of neurotrophins by pulp fibroblasts upon carious injury. Recently we demonstrated that caries-associated C5a receptors (C5aR) expression is followed by its activation by the C5a generated from the activation of complements molecules expressed by pulp fibroblasts. C5aR signaling results in brain-derived nerve growth factor (BDNF) secretion by pulp fibroblasts that induces prominent neurite outgrowth toward the site of carious injury. Previously another C5a receptor, C5L2, has been identified. Since no signaling pathway is induced following its interaction with C5a, it received very little attention. In this study, our results further demonstrate that newly generated C5aR in human pulp are co-localized with C5L2 both *in vivo* and *in vitro* shortly after carious injury. Furthermore, C5L2 siRNA-silencing significantly increased BDNF-secretion in LTA-stimulated pulp fibroblasts. Thus the C5aR and C5L2 studies in the regenerative process could provide innovative therapeutic strategy, i.e., the possibility to enhance and/or prolong the positive action of C5a in dental pulp regeneration by activating or blocking these active and inactive receptors.

Biography

Fanny Chmilewsky has completed her PhD in 2013 from Aix-Marseille University and currently doing postdoctoral research from University of Illinois at Chicago College of Dentistry. She has exemplary training in pulpal biology with expertise in pulp regeneration and complement system research. She has published her research in very reputed journals such as Journal of Dental Research and American Journal of Pathology.

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