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OR.77. The MAPK Pathway Uses MKP-1 and c-Fos to Discriminate Pathogenic from Commensal States of Candida Albicans in Oral Epithelial Cells

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Host mechanisms enabling discrimination between commensal and pathogenic organisms are critical in mucosal immune defense and homeostasis. The polymorphic fungal pathogen Candida albicans can act as a commensal or pathogen. We demonstrate that oral epithelial cells orchestrate the innate response to this fungus via NF-κB and a biphasic MAPK response. The response of an oral epithelial cell line to *C. albicans* was determined using western blotting, ELISA and microbead assays. *C. albicans* activated both the NF-κB and MAPK pathways, including the MKP-1 phosphatase. Whilst NF-κB activation was linear, MAPK activation was biphasic, with peaks at 15 minutes and 2 hours. Inhibition of these pathways affected production of different cytokines and genes in response to infection. Only hyphal forms of *C. albicans* activated the second MAPK phase, which constitutes MKP-1 phosphorylation, activation of the transcription factor c-Fos, and induction of a pro-inflammatory responses, leading to a protective host phenotype. The yeast phase subverts the biphasic MAPK/MKP-1/c-Fos response resulting in the absence of inflammatory mediators, thus permitting the fungus to colonize mucosal surfaces without host challenge. We therefore propose a mechanism enabling epithelial cells to distinguish between commensal and pathogenic organisms through selective activation MKP-1 and c-Fos.

OR.78. Nasal Vaccine Adjuvant Activity of Interleukin 1 Alpha (IL-1α) is Dependent upon IL-1-responsive Bone Marrow Derived Cells

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IL-1α is an effective adjuvant for nasally delivered vaccines, but its mechanism of action is poorly characterized. To determine the cellular compartment required for IL-1α adjuvant activity, we generated IL1R bone marrow chimeric mice that contained adjuvant-responsive stromal cells with adjuvant-unresponsive bone marrow-derived cells (IL1RKO→SJL) or adjuvant-unresponsive stromal cells with adjuvant-responsive bone marrow-derived cells (SJL→IL1RKO). Mice were vaccinated with 50 μg Bacillus anthracis lethal factor (LF) alone or with 4 μg IL-1α or 1 μg cholera toxin (CT) on days 0, 7, 21, and 42. IL1RKO→IL1RKO mice vaccinated with LF+IL-1α had similar responses to LF alone. At day 56, serum IgG titers were not different in the IL1RKO→SJL, SJL→IL1RKO, or SJL→SJL chimeric groups vaccinated with LF+CT or LF+IL-1α, but both treatments were increased over LF alone ($p<0.05$). LeTx neutralizing antibody titers (NT) were also measured at day 56. LF+CT induced an increase over LF alone in NT for all chimeric groups ($p<0.05$). LF+IL-1α and LF+CT induced similar NT in SJL→IL1RKO and SJL→SJL chimeras. In IL1RKO→SJL animals, LF+CT induced a higher NT than LF+IL-1α ($p<0.01$). Day 56 mucosal IgA titers demonstrated a similar trend. These data suggest that adjuvant-responsive bone marrow cells are required for maximal adjuvant activity of IL-1α when delivered nasally.

OR.79. Alterations in the Salivary Proteome During Periodontal Inflammation

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As a site of high pathogen exposure, the oral cavity has a variety of mechanisms to inhibit pathogen colonisation, including the expression of soluble defence proteins from the oral mucosa and salivary glands. To identify proteins which may be altered during oral inflammation, we used quantitative proteomics to investigate whole saliva from nine individuals with severe periodontal disease, comparing their proteomic profile before and after periodontal treatment. A comparison of 128 proteins across all saliva samples identified fifteen protein spots with altered abundance. The predominant alteration observed was an increase in the abundance of the S100 proteins S100A8/A9 (calprotectin) and S100A6. Two acute phase response proteins, haptoglobin and transthyretin, were also identified. Of the remaining proteins with altered abundance, prolactin inducible protein and parotid secretory protein have previously been associated with host defence, while the function of the ubiquitous intracellular proteins transketolase, transaldolase and GDP-dissociation inhibitor B is less clear, but may reflect cellular damage in the inflamed gingiva. These results highlight the predominant involvement of S100 proteins in the host response during periodontitis, identify host defence components which have not previously been linked to this disease and suggest new potential biomarkers for monitoring disease activity in periodontitis.

OR.80. NALT Derived-DCs Induce Innate B1-B Cells to Undergo IgA Class Switching Recombination

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In previous studies, T cell-independent secretory IgA Ab responses were seen in saliva and nasal washes of mice given nasal TNP-LPS plus cholera toxin (CT). Here, we tested the hypothesis that mucosal dendritic cells (DCs) play a central role in the induction of IgA class switch recombination (CSR)

in mucosal B1-B cells. When mice were nasally immunized with TNP-LPS plus CT as mucosal adjuvant, DCs from nasal passages (NPs), submandibular glands (SMGs) and NALT showed high levels of a proliferation-inducing ligand (APRIL)-specific mRNA, while mucosal B1-B cells showed significant levels of transmembrane activator and calcium modulator cyclophillin ligand (TACI)- and B cell maturation antigen (BCMA)-specific mRNA. Further, when splenic surface IgA-, IgM+ B cells were stimulated with DCs from NPs, SMGs or CLNs of mice given nasal LPS plus CT, a high frequency of IgA+ B cells were induced. These findings suggest that DCs in mucosal effector tissues originally derived from NALT are activated by CT and promote B1-B cell IgA CSR through APRIL/BMCA and APRIL/TACI interactions. This ongoing work is supported by NIH grants DE 12242, AG 025873 and AI 18958 as well as by Grants-in-Aid (C-19592403) from the Ministry of Education, Culture, Sports, Science and Technology of Japan.