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381
Seroncoversion after anti-SARS-CoV-2 mRNA vaccinations among moderate-to-severe psoriatic patients receiving systemic biologicals

EA Pipaluk1, SA Pereiro2, JG Chéret1,2, MS Collins3, RP Asakawa4, S Shimada5, R Paus1,2 and MM Senna6

We here report a prospective study of 33 seronegative (SN) psoriatic patients (median age: 54 [44.1-66.6] years) who were included in our study for 21 days after the administration of the second dosage of BNT162b2 or mRNA-1273 vaccine, antibody levels specific to the SARS-CoV-2 spike (S) protein receptor binding domain were detected in 21 days after the administration of the second dosage of mRNA vaccine in moderate-to-severe psoriatic patients receiving biologicals, similar to those of healthy controls.

382
Environmental pathology of frontal fibrosing alopecia (FFA): Does linalool promote bulge immune privilege (IP) of elderly?

J Gherradini1, J Chéret2,3, MS Collins1, R Paus1,2 and MM Senna1

The presence of ILC2 may suggest the pathophysiological contribution to FFA. To investigate this, we exposed FFA biopsies to linalool to see if it could affect IP of FFA.

383
The presence of ILC2 may suggest the pathophysiological contribution to eosinophilic pustulosis folliculitis

T Kagome1, T Takegami1, P Bhardwaj2, T Nomura and K Kabashima4

Eosinophilic pustulosis folliculitis (EPF) is a disease with unknown etiology, which is characterized by symptoms, including eosinophilic pustules on the face and other hair follicles.

384
TNF is partially required for cell-death-triggered skin inflammation upon acute loss of cFLIP

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cFLIP is required for epidermal integrity and skin inflammation silencing via protection from TNF-induced keratinocyte apoptosis. Here, we generated and analyzed cFLIP deficient keratinocytes with additional TNF deficiency. Intriguingly, the ablation of TNF rescued the pathological phenotype of epidermal cFLIP KO from characteristic weight loss and increased mortality. Moreover, the lack of TNF in these animals strongly reduced and delayed the epidermal hyperkeratosis and the increased apoptosis in keratinocytes. Our data demonstrate that TNF signaling in cFLIP-deficient keratinocytes is the critical target for the regulation of skin inflammation via modulated cytokine and chemokine expression and, thus, the attraction of immune cells. Our data suggest that autocrine TNF loop activation upon cFLIP depletion is critical for keratinocyte apoptosis induction and provides evidence for a negative regulatory role of cFLIP for TNF-dependent apoptosis and partially for epidermal inflammation. However, alternative signaling pathways may contribute to the development of the dramatic skin disease upon cFLIP deletion. Our data warrant future studies of the regulatory mechanism controlling the development of skin disease upon cFLIP deficiency and the role of cFLIP/TNF in a number of inflammatory skin diseases, including toxic epidermal necrolysis (TEN).

385
Purinergic molecules in murine mast cells

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In the skin, adenosine triphosphate (ATP) is released from various types of cells by various environmental stimuli via nonsynthetic mechanisms, cell damage, or acute cell death. Because ATP is a potent inducer of skin inflammation, it has to be promptly hydrolyzed for the skin to achieve homeostasis. Of note, ATP activates mast cells (MCs) through P2X7R, leading to the enhanced skin inflammation. However, MC involvement in the impairment of skin inflammation via ATP hydrolysis remains largely unknown. Thus, we sought to determine the expression of ATP-hydrolyzing molecules in MCs. Bone marrow- and fetal skin-derived MCs (BM-MCs and FSC-MCs) were used in the study. A culture of BM-MCs and FSC-MCs with 1 mM ATP-γ-S, a non-metabolizable ATP analogue, or 1 μM ionomycin for 60 min or 10 min, respectively, induced their degranulation. PGE2-treated steady-state BM-MCs and FSC-MCs strongly expressed mRNA of Entpd1 (CD19) that potently hydrolyze ATP. While both the ATP-γ-S and ionomycin upregulated Entpd1 (CD19) mRNA expression. Moreover, BM-MCs, FSC-MCs from young donors, and BM-MCs from back skin of Bin2 female mice clearly expressed Entpd1 (CD19) at protein levels. Exogenous ATP (1000 μM) was added in the culture of PBS- or ionomycin-treated BM-MCs and FSC-MCs to check whether Entpd1 (CD19) on murine MCs is functional. BM-MCs and FSC-MCs hydrolyzed ATP. In addition, ionomycin-treated murine MCs tended to increase ATP hydrolyzation. These data suggest that MCs participate in ATP hydrolysis via Entpd1 (CD19). Moreover, degranulated murine MCs trended towards increase of ATP-hydrolyzing activity. Collectively, murine MCs express functional ATP-hydrolyzing molecules, thereby contributing to achieve skin homeostasis.

386
The Adaptive Response of Old ABCB5+ MSCs is Changed Upon Exposure to LPS

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Mesenchymal stem cells (MSCs) are endowed with the unique capacity to raise an adaptive response to environmental cues. This allows MSCs to control their direct neighbourhood and the surrounding tissue niche. Upon exposure of MSCs with infection mimicking lipopolysaccharide (LPS), MSCs completely shift their transcriptome with the release of neutrophil activating chemokines. The LPS induced transcriptomic shift resulted in a significant increase of neutrophil activated mRNA transcripts (mRNA) and proteolytic enzymes. This adaptive response guarantees the defense from bacterial attack. Wound healing decreases with age and propensity for infection increases. Therefore, we addressed the question whether MSCs from old healthy donors (> 65 years) unlike young healthy donors (< 30 years) may change their response upon LPS exposure towards a reduced microbialidal response. (Cultured ABCB5+ MSCs from young and old donors treated with LPS revealed differences in the time kinetic of NF-κB translocation from the cytoplasm to the nucleus. By contrast to ABCB5+ MSCs from young donors, ABCB5+ MSCs from old donors delayed the NF-κB nuclear translocation. Intriguingly, the lack of nuclear NF-κB translocation, supported by an overexpression of p-IκBα. This correlates with a higher and longer persisting expression of NF-κB target genes like IL-6 in MSCs of elderly individuals compared to young individuals. Notably, ABCB5+ MSCs from young donors depict higher expression levels of IL-8 and IL-10 compared to old donors. Of note, LPS primed ABCB5+ MSCs from young donors can activate neutrophils by producing NETs to a higher level in comparison to old donors. NE activity indicative for microbicidal activity of ABCB5+ MSCs was lost when PMA stimulated neutrophils is significantly higher and LPS-concentration-dependent compared to old donors. Collectively, MSCs from old individuals reveal a dysregulated anti-bacterial response which is supported by an impressively reduced killing ability of gram negative bacteria and at least in part explained higher susceptibility for severe bacterial infections in elderly.

ABSTRACTS | Innate Immunity and Inflammation

S246 Journal of Investigative Dermatology (2022), Volume 142

ATP-hydrolyzing molecules in MCs. Bone marrow- and fetal skin-derived MCs (BM-MCs and FSC-MCs) were used in the study. A culture of BM-MCs and FSC-MCs with 1 mM ATP-γ-S, a non-metabolizable ATP analogue, or 1 μM ionomycin for 60 min or 10 min, respectively, induced their degranulation. PGE2-treated steady-state BM-MCs and FSC-MCs strongly expressed mRNA of Entpd1 (CD19) that potently hydrolyze ATP. While both the ATP-γ-S and ionomycin upregulated Entpd1 (CD19) mRNA expression. Moreover, BM-MCs, FSC-MCs from young donors, and BM-MCs from back skin of Bin2 female mice clearly expressed Entpd1 (CD19) at protein levels. Exogenous ATP (1000 μM) was added in the culture of PBS- or ionomycin-treated BM-MCs and FSC-MCs to check whether Entpd1 (CD19) on murine MCs is functional. BM-MCs and FSC-MCs hydrolyzed ATP. In addition, ionomycin-treated murine MCs tended to increase ATP hydrolyzation. These data suggest that MCs participate in ATP hydrolysis via Entpd1 (CD19). Moreover, degranulated murine MCs trended towards increase of ATP-hydrolyzing activity. Collectively, murine MCs express functional ATP-hydrolyzing molecules, thereby contributing to achieve skin homeostasis.