

Cytosolic Ca²⁺ signals are performed by Ca²⁺ releases from the endoplasmic reticulum and Ca²⁺ influx from the extracellular medium. Releases rely on the refilling of the intracellular Ca²⁺ stores by the Ca²⁺ influx "Store Operated Ca²⁺ Entry" (SOCE) via the channel Orai1. Here we show that Orai1 expression, SOCE amplitude and epidermal proliferation are decreased in the epidermis of patients with dermatoporosis when compared to aged non-atrophic skin. Epidermal atrophy was induced in mice by the inhibition of Orai1 with small interfering RNA and the topical application of a SOCE blocker, BTP2. The inhibition of Orai1 impaired the HB-EGF-induced Ca²⁺ signals and fully prevented the mitogen effect of HB-EGF in vitro. Importantly, keratinocyte proliferation correlated with SOCE amplitude in vitro and Orai1 expression in vivo regardless of the method used to inhibit SOCE (chemical inhibitor or genetic knockdown). Conversely, the topical application of SOCE-activators increased epidermal thickness and proliferation in mice while the pro-proliferative effect of SOCE-activators was prevented by the inhibition of Orai1 in cultured keratinocytes. Finally, the topical application of SOCE-activators reversed the epidermal atrophy induced by corticosteroids in mice. The topical modulation of Ca²⁺ signals is thus a new and promising therapeutic strategy in dermatology.

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Birhombic flap – a modified bilobed flap - for repair of nasal defect

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Background: Skin cancer of the nose is frequent. Surgical reconstruction of longitudinal defects of the lateral nasal alar might be a challenge and has to be performed with prudence. The nose, due to its prominent pyramid like shape with two symmetrical alar wings, has a high potential risk of retraction and consequent asymmetry. Loss of this symmetry and/or washed out nasal sulcus can result in loss of identity. Second healing intention, a full thickness skin graft and/or multiple rotation and transposition flaps can be considered and are well described in literature. A classical bilobed flap is commonly used for round defects.

Objective: We describe a birhombic flap, characterized by a combination of transposition and rotation movement at the same moment, used for longitudinal defect of the lateral nasal alar.

Methods: Demonstration of the technique and practical application for this kind of reconstruction. **Results:** The classical bilobed flap is a very useful for reconstruction of round defects on the lateral nasal tip or distal alar. We show that a small modification of the flap allows to cover also longitudinal defects on the lateral tip of the nose. As the first lobe movement corresponds more to the rhomboid transposition flap we prefer to call it birhombic flap. We insist on the point that for most nasal alar defects the pedicle of the flap should be placed medially. Otherwise

the flap crosses the border of two anatomic subunits (ala nasi and lateral nasal sidewall) which correspond to the concave sulcus nasi. This would result in filling out the concavity of the this most important anatomic landmark when the defect is not placed nearly on the tip of the nose. In general in this case the rotation point of the second lobe of this flap is placed so that - in the situation of medial pediculation - it allows also to recreate the convexity of the supratip which is a second most important landmark of the nose.

Conclusion: The birhombic flap has its place in reconstructive surgery. This flap has a specific indication and precise advantage compared to other repairs in particular to the classical bilobed flap. This kind of reconstruction is well adapted to the concept of anatomic subunits. It allows to create the convexity of the supratip of the nose with an excellent aesthetic outcome.

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CXCR3 ligands recruit plasmacytoid dendritic cells and stimulate type I IFNs production during cutaneous wound healing

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Plasmacytoid dendritic cells (pDCs) are specialized immune cells that can sense the presence of microbial nucleic acids through the expression of the endosomal toll-like receptor (TLR) 7 and TLR9, leading to the production of type I IFNs. It is now well established that cathelicidin peptides produced by keratinocytes can complex with self-DNA and self-RNA and transport them into endosomal compartments, converting inert host-derived nucleic acids into potent pDCs activating factors. We have shown that such a mechanism could explain the sustained pDC activation and production of type I IFNs in psoriasis as cathelicidin peptides are overexpressed in psoriatic skin. Interestingly, we observed that skin injury triggers a transient infiltration of pDCs that produce IFN- α/β , participating to the acute inflammatory response occurring during wound healing. Activation of pDCs likely involves the recognition of self-nucleic acids released by skin damaged cells. Although cathelicidin peptides are sufficient for this stimulation, they are not required for the type I IFN production observed, suggesting the presence of other factors that can activate pDCs in skin wounds. Moreover, the mechanism by which pDCs are recruited to the injured skin remains to be determined. To sort out the potential factors involved in the recruitment and stimulation of pDCs to the site of injury, we analyzed the gene expression of mouse skin by microarray at different time points following skin injury. Among the different chemokines whose receptors are expressed by pDCs, only the CXCR3 ligands CXCL9, CXCL10, and CXCL11 had an expression paralleling pDCs infiltration. Intradermal injection of CXCR3 ligands in mice was sufficient for the recruitment of pDCs in the skin and the production of IFN- α/β , suggesting that they may contribute to the wound healing process. Similarly to the cathelicidin peptides, CXCR3 ligands could form complexes with DNA that can be uptaken by pDCs and