# The Editor's Choice

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## Targeted next-generation sequencing of matched localized and metastatic primary high-risk SCCs identifies driver and co-occurring mutations and novel therapeutic targets

Cutaneous squamous cell carcinoma (SCC) is the second most common type of skin cancer. While only 3-5% of SCCs metastasize, those that do are associated with significant morbidity and mortality. Using gene mutations to help predict metastasis and select therapeutics is still being explored. Lobl M et al presented novel data from targeted sequencing of 20 case-matched localized and metastatic high-risk SCCs. Using spatial clustering analysis, primary driver mutations were identified as EGFR in localized SCC and CDH1 in metastatic SCC. ERBB4 and STK11 were found to be significant cooccurring mutations in localized SCC. Pathway analyses showed the RTK/RAS, TP53, TGF-b, NOTCH1, PI3K, and cell cycle pathways to be highly relevant in all high-risk SCCs with the Wnt pathway enhanced in metastatic SCC only.

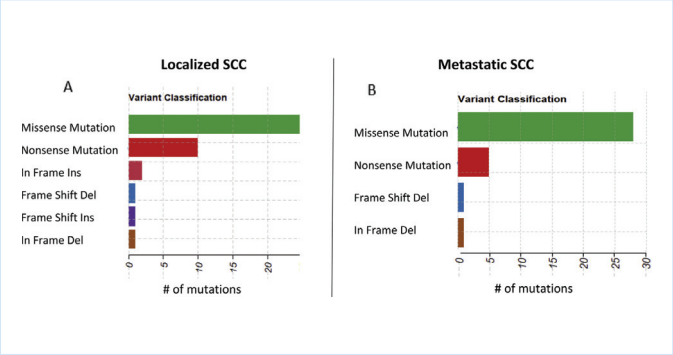


**Fig. 1.** Summaries of mutations in localized and metastatic SCC. A and B-These plots illustrate variant classifications in localized and metastatic SCC.

## Involvement of adaptor protein Disabled-2 on skin fibrosis in systemic sclerosis

Systemic sclerosis (SSc) is a connective tissue disease characterized by inflammation and fibrosis. Disabled-2 (DAB2) expression was significantly downregulated by salvianolic acid B, a small molecular medicine which attenuated experimental skin fibrosis of SSc. These suggest that DAB2 plays an important role in SSc skin fibrosis. Mei X et al investigated the role of DAB2 in SSc. DAB2 expression was enhanced in SSc lesion skin and was positively correlated with fibrotic genes, such as α-SMA and PAI-1. The in vivo study revealed that DAB2 downregulation alleviated skin fibrosis, alleviating skin thickness and reducing collagen deposition, and DAB2 knockdown ameliorated the inflammatory cell infiltration. The in vitro study showed that DAB2 knockdown reduced extracellular matrix genes and proteins expression. Moreover, Transcriptome analysis revealed TGF-β and focal adhesion signaling pathways were the main downregulated pathways involved in DAB2 siRNA treated fibroblasts. DAB2 played an important role in the pathogenesis of SSc and DAB2 modulation may represent a potential therapeutic method for SSc.

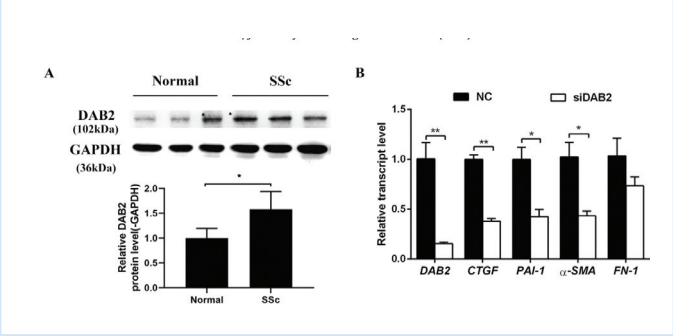


**Fig. 4.** The effect of DAB2 knockdown in SSc skin fibroblasts. (A) The expression of DAB2 in cultured normal (n = 3) and SSc skin fibroblasts (n = 3). (B) Relative transcript levels of *DAB2*, *CTGF*, *PAI-1*, α-*SMA* and *FN1* in the different treatment groups (n = 6).

## Short-term effectiveness of biologics in patients with moderate-to-severe plaque psoriasis: a systematic review and network meta-analysis

Complete lesion clearance is important to patients with psoriasis. Tada Y et al conducted a network meta-analysis of randomized controlled trials of biologic agents available for psoriasis in Japan, using mixed-treatment comparisons. Data were pooled from 41 trials in 19,248 patients. All biologics were significantly more effective than placebo for PASI100, PASI90 and PASI75. The RD for PASI100 for brodalumab vs ixekizumab was 0.05 (95% Confidence intervals [CI] −0.02, 0.11), brodalumab vs risankizumab was 0.04 (95%CI −0.03, 0.11), and risankizumab vs ixekizumab was −0.01 (95%CI −0.08, 0.06). The SUCRA for PASI100 and PASI90 achievement was 96.8% and 86.8%, respectively, for brodalumab, 82.6% and 90.3%, respectively for risankizumab, and 78.3%, 80.9%, respectively, for ixekizumab. Of the biologics assessed, brodalumab, ixekizumab and risankizumab were the greatest rates of PASI90 and PASI100 achievement, and a higher probability of being most effective in the induction phase, compared with the other biologics.

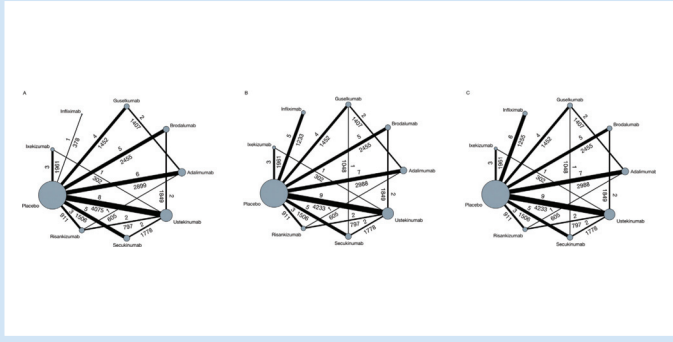

**Fig. 2.** Network graph of all eligible comparisons for (A) Psoriasis Area and Severity Index (PASI) 100, (B) PASI90, and (C) PASI75. The size of the nodes and the thickness of the lines are weighted according to the number of patients. Each line connecting 2 nodes indicates a direct comparison. The number above each line indicates the number of studies in that comparison, and the number below each line indicates the total number of patients enrolled into the relevant studies.