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Medicine

Gene Expression Analysis of Atypical Fibroxanthoma Patients Reveals New Insights into the Tumor Microenvironment

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Introduction

Atypical Fibroxanthoma	• Rare low grade superficial carcinoma
Background	• Less aggressive than undifferentiated pleomorphic sarcoma • Sun exposed areas of the body • Ultraviolet light induction • Mohs surgery
Cell origin	• Unclear • Previously proposed Fibroblast origin
Purpose	• Expand current knowledge on AFX microenvironment and tumor origin • Analysis of data set comprising 8 superficial cutaneous papules and nodules of AFX excised by Mohs surgery and subjected to cell deconvolution analysis and pathway analysis.[2]
Hypothesis	• We hypothesized that the cellular origin of AFX is of epithelial or keratinocyte origin.

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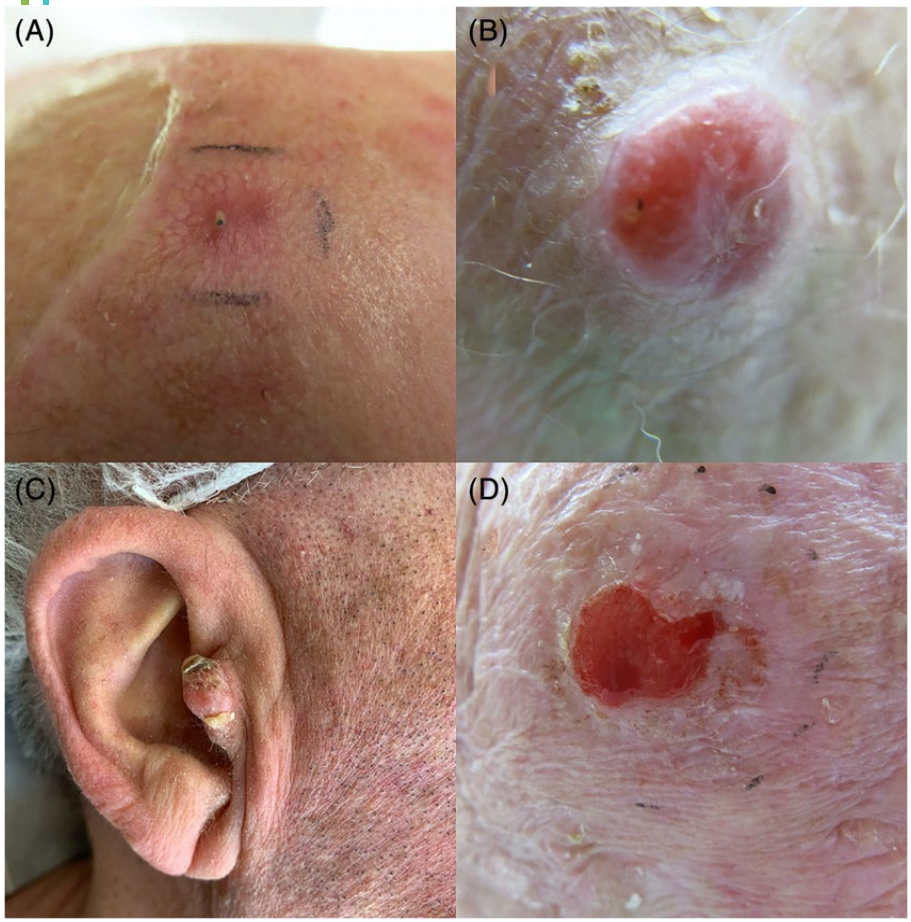
2.
Lai, K., et al. (2017). Genomic analysis of atypical fibroxanthoma. *PloS one*, *12*(11), e0188272.

Clinical Presentation



(A) Ill-defined small plaque on the scalp.

(B) Flesh-colored nodule surrounded by actinic keratoses.

(C) Keratotic nodule on the tragus.

(D) Eroded plaque on elastotic scalp.

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Bitel, A., et al. (2020). Atypical Fibroxanthoma – An Analysis of 105 Tumors. Dermatologic Therapy. 33. 10.1111/dth.13962

Methods

RNA-Sequencing paired expression data on AFX by Lai *et al.* (GSE85671)

- We analyzed publicly available RNA-sequencing data from eight AFX patient tumor tissues and paired histologically normal tissues bordering the lesion after successful excision by Mohs surgery.

Cell Deconvolution

- Analyze genetic component of cells to ascertain cell origin
- Analysis based on RNA sequencing
- Analysis was performed using xCell package in R to ascertain AFX cell-type composition and immune cell microenvironment as well as controls.
- Gene analysis utilized for computational estimation of different cell types.

Pathway Analysis (GSVA)

- Used to analyze the cell makeup of the tumor tissue compared to normal tissue
- Gene set variation analysis (GSVA) utilized to pinpoint cellular pathways upregulated or downregulated
- Whether gene set is upregulated or downregulated as a whole

Cell Deconvolution

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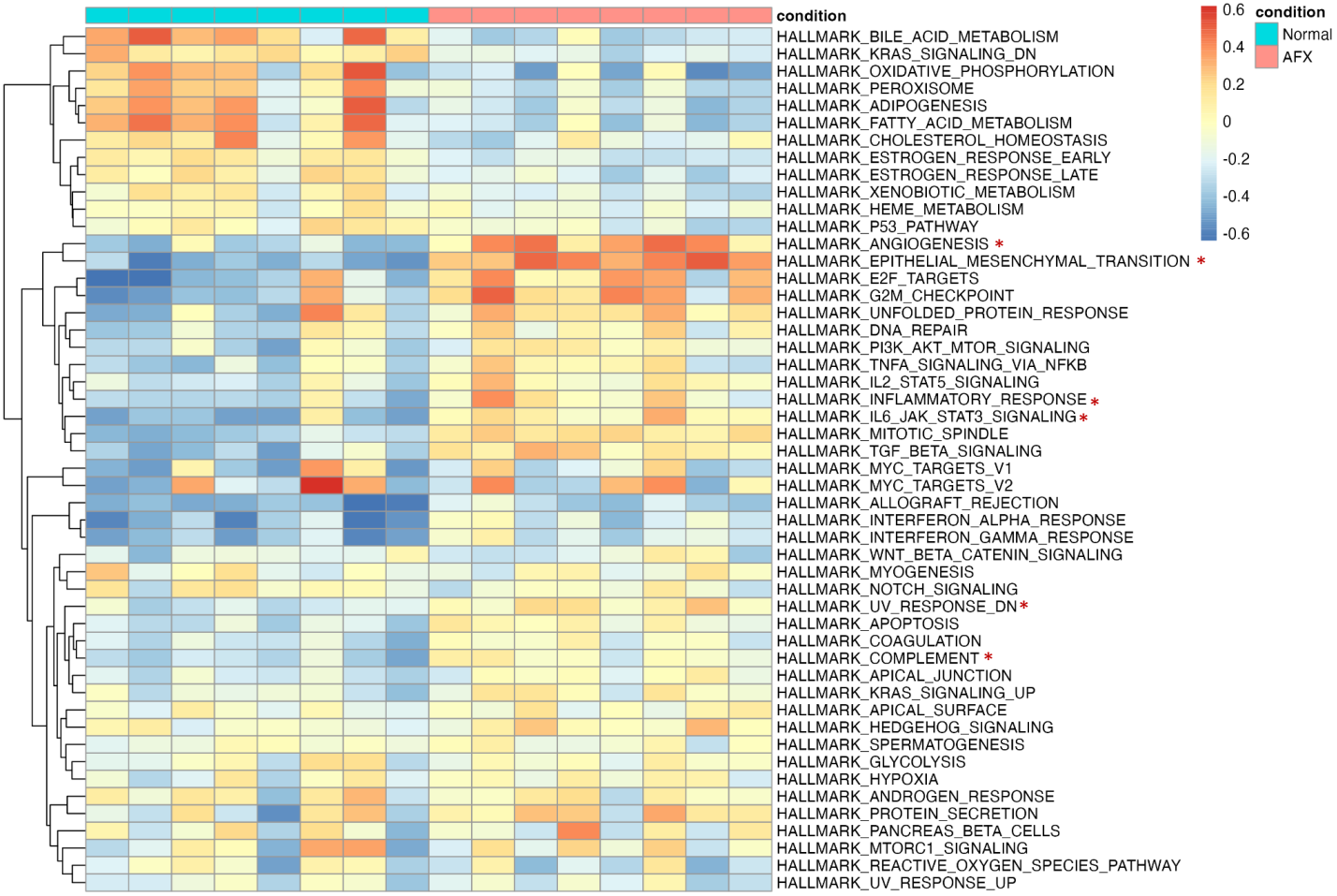
Pathway Analysis (GSVA)



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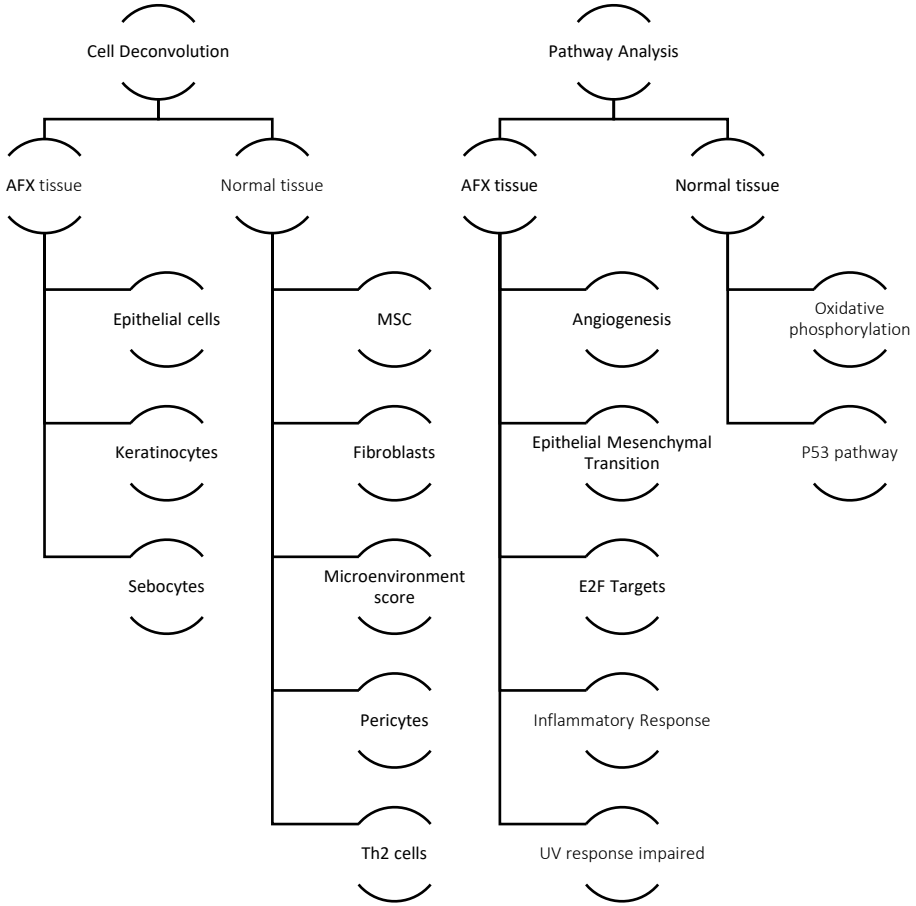
Results



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Discussion

- The cellular origin of AFX is currently unclear. The characteristic spindled cells found in AFX tissue have been hypothesized to be EMT-transitioned keratinocytes (Mirza & Weedon, 2005; Nakamura *et al.*, 2010)
- Our cell deconvolution revealed an enriched presence of Epithelial cells, keratinocytes, and sebocytes within the AFX tissue lesions.
- On the contrary, the bordering normal tissue had enrichment of Mesenchymal Stem Cells, and Fibroblasts, as well as Type II Helper T cells.
- EMT and Inflammatory response pathways were upregulated in AFX tissue.
- There was no infiltration of macrophages or other immune cells revealed by cell deconvolution, which was otherwise reported previously by the Arron group (Lai *et al*, 2017).

Conclusion and Future Prospect

- Our computational analyses suggest that AFX may be of epithelial rather than fibroblast origin.
- Presence of immune cell infiltration surrounding AFX tumors.
- Increase in the presence of inflammatory pathways in AFX tumor tissue.
- Expanding on previous findings is integral to develop treatment approaches and to better understand the prognosis of AFX.
- Future prospects would focus on investigating mitochondrial dysregulation and the possible molecular drivers of AFX.

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