APOBEC3B in Premalignant and Malignant Skin Tumours:
An Immunohistochemical Profile

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INTRODUCTION

Skin cancer belongs to the most common malignancies worldwide, with rising incidence[1]. It includes keratinocyte (non-melanoma) skin cancers such as basal cell carcinoma and squamous cell carcinoma, as well as malignant melanoma, which is less frequent but more aggressive[1].

Although **ultraviolet radiation (UV)** remains the main etiological factor, it does not fully explain the mutational landscape[1]. Additional contributors include the **APOBEC** (**apo**lipoprotein **B** mRNA-**e**diting **c**atalytic polypeptide-like) family of cytidine deaminases[2]. Among these enzymes, **APOBEC3B (A3B)** is linked to high mutation rates and disease progression in several cancers, including breast and cervical cancer[2,3]. Overexpression of A3B is associated with an aggressive clinical course, worse prognosis, and therapy resistance across different cancer types[2,4]. This makes A3B a promising candidate to study as a source of genomic instability in skin cancer.

KEY WORDS

APOBEC, skin cancer, immunohistochemistry

The **AIM** of this study is to investigate the expression pattern of A3B across benign and malignant skin lesions, and to compare its expression profile in keratinocyte- versus melanocyte-derived tissues.

METHODS

Tissue Samples → **Sectioning** → **Immunohisto-chemistry** → **Image Analysis** → **Statistics**

Archived tissue blocks from benign, premalignant and malignant keratinocyte- as well as melanocyte-derived skin tissues were investigated for the expression of A3B (n = 67).

Thin sections (4-6µM) were cut and mounted on glass slides.

All sections were stained using the anti-A3B antibody (Abcam, ab191695) on the Epredia Autostainer 360, with HRP/DAB detection and hematoxylin counterstaining.

Sections were digitized (Aperio scanner). Regions of interest were annotated by a dermatopathologist. Automated cell detection in QuPath was verified by blinded manual analysis.

RStudio software was used for statistical analysis.

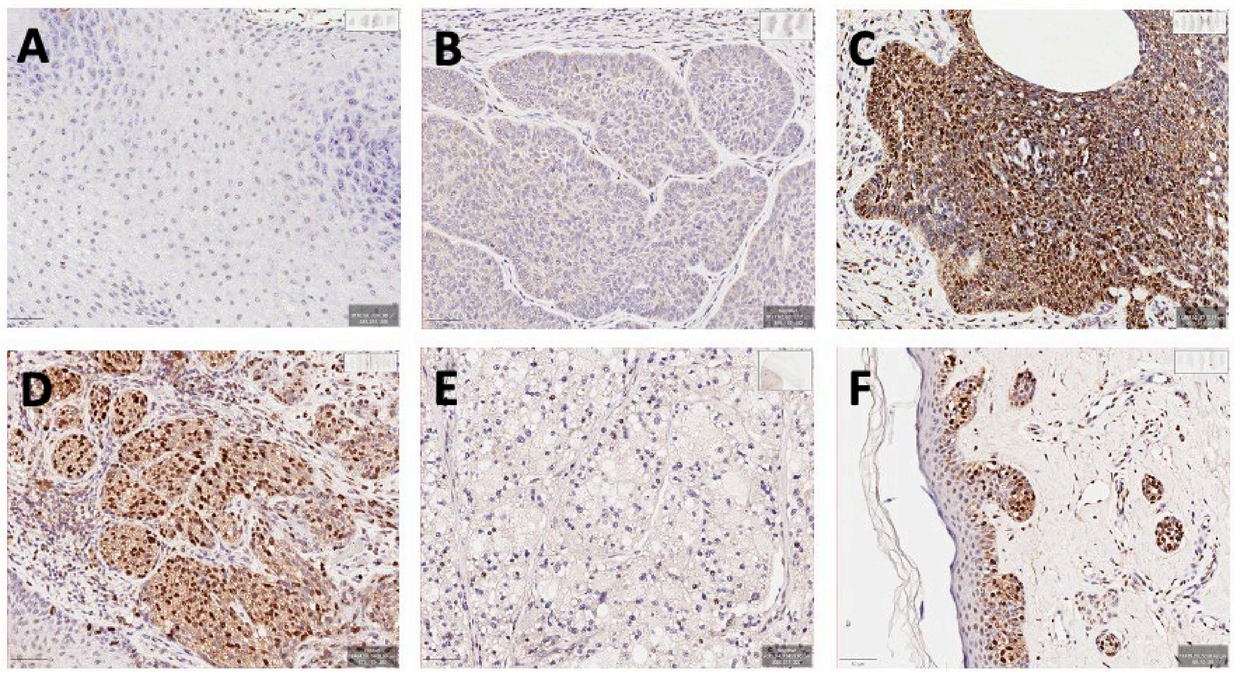

Figure 1: A3B expression in representative skin tissues
A. Negative cutaneous squamous cell carcinoma sample.
B. Negative basal cell carcinoma sample.
C. Basal cell carcinoma showing intense nuclear A3B staining in the vast majority of the cancerous cells.
D. Superficial spreading melanoma exhibiting strong nuclear A3B expression in melanocytic nests.
E. A3B-negative nodular melanoma.
F. Benign nevus with numerous positive melanocytes in the basal layer of the epidermis and positive dermal nests.

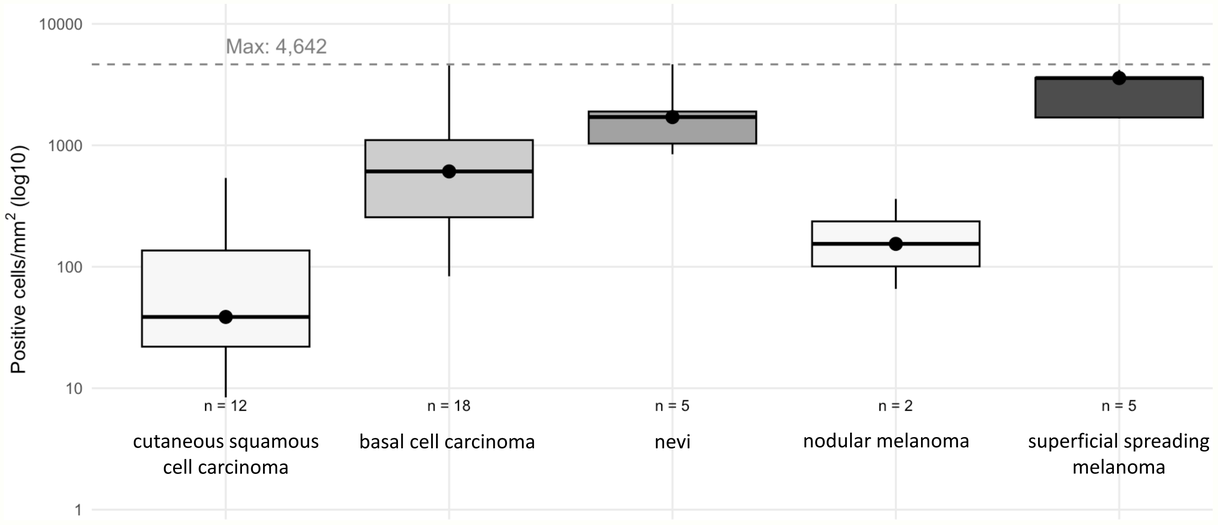

Figure 2: Box plot showing nuclear A3B expression (positive cells per mm2, log10 scale) across different skin tissues. Interquartile range, median, minimum and maximum values are shown. Keratinocyte-derived lesions are displayed in light grey, melanocyte-derived lesions in dark grey.

RESULTS

In general, keratinocyte-derived non-melanoma skin cancers had lower expression than melanocyte-derived skin tissues:

- **Very low numbers** of A3B-positive cells were found in cutaneous squamous cell carcinoma.
- Basal cell carcinomas showed **intermediate expression** with a median around 1000 cells/mm². There were no major differences between nodular (mean of 1066.91 ± 1307.62) and superficial (973.56 ± 1420.33) subtypes.
- The **highest expression** overall was observed in melanocytic proliferations. Benign and dysplastic nevi showed similar levels, whereas malignant melanoma subtypes differed: superficial spreading melanomas were consistently highly positive, while nodular melanomas were negative. The highest individual value was seen in a nevus on the lower leg (4642 cells/mm²).

Our data shows a significant difference in A3B expression between melanocytic and keratinocytic skin tissues ($p < 0.0001$). While A3B is consistently present in melanoma and occasionally high in basal cell carcinoma, it appears largely absent in cutaneous squamous cell carcinoma.
These findings point to a potential role in tumour development and support further investigation of A3B as a biomarker, and possibly a therapeutic target, in skin cancer.

FUTURE PERSPECTIVES

- **Larger cohort:** The validation of our findings in a larger cohort is required.
- **Basal cell carcinoma:** A3B expression shows strong variability. SOX-10 co-staining would help to define the cellular origin.
- **UV effects:** UV may contribute to A3B-mediated mutagenesis, but current evidence is limited and mainly derived from other APOBEC family members.
- **Immune context:** Immune-related signals (e.g. T-cell activity, interferon release) could influence A3B expression and need to be addressed.
- **Therapy relevance:** APOBEC-associated mutations (e.g. PIK3CA, MEK2) in melanoma indicate a potential impact of A3B on therapy response or resistance.

References

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