

# Association of HLA haplotypes with Fibroids, Keloids and Hypertension risk: A Review

Chloe Odusola<sup>1</sup>, Kennedy Cruickshank<sup>1</sup>, Tanya Shaw<sup>1</sup>, Andrew Webb<sup>1</sup>

<sup>1</sup>King's College London

## BACKGROUND

Fibrosis is the excess deposition of extracellular matrix components at sites of damage in the body leading to tissue thickening or scarring. It affects multiple systems within the body, this review was to assess the mechanisms by which fibrosis leads to the development of hypertension, keloids and fibroids.

These conditions all disproportionately affects women of African/Caribbean descent and may share genetic and immunological risk factors, particularly in the HLA gene region.

The human leukocyte antigen (HLA) system is a highly variable group of immune-related genes that help the body recognise foreign substances. Certain HLA class II variants may influence fibrotic disease risk through immune-mediated pathways.

## AIMS/OBJECTIVES

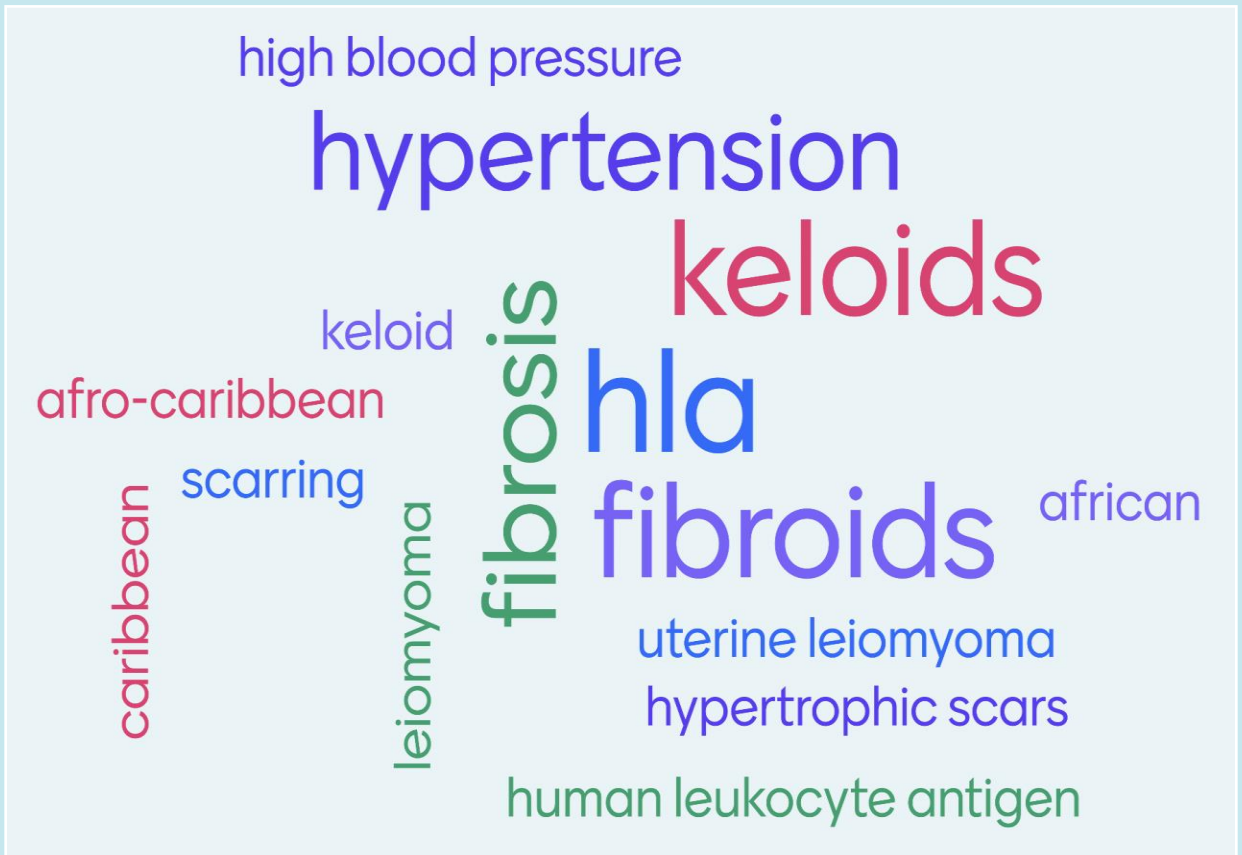
This literature review assessed two main concepts:

- Do HLA genes play a role in causing fibrosis?
- Is there a shared HLA gene increasing the risk of developing hypertension, keloids and uterine fibroids?

## METHODS

Scholarly articles were obtained from **MEDLINE**, **PubMed** and **Google Scholar** using keywords included in the word cloud.

They were included if published in English and assessed HLA haplotypes in the relevant three conditions.



## RESULTS: KELOIDS

Keloids: excess ECM deposition forming benign raised scars, expand horizontally beyond injury borders, no regression.

Results:

- Significant positive associations found in **HLA-DRB1**, **DQA1** and **DQB1** alleles – **higher risk**.
- Significant negative associations found in different **HLA-DQA1** and **DQB1** alleles – **protective** OR lower risk.
- HLA-DRB1 allele association in Northern European populations, vs others in Chinese Han populations.
- Findings not yet replicated in African and Caribbean populations.
- Possible mechanism: stronger antigen presentation → excessive immune response → excessive collagen deposition

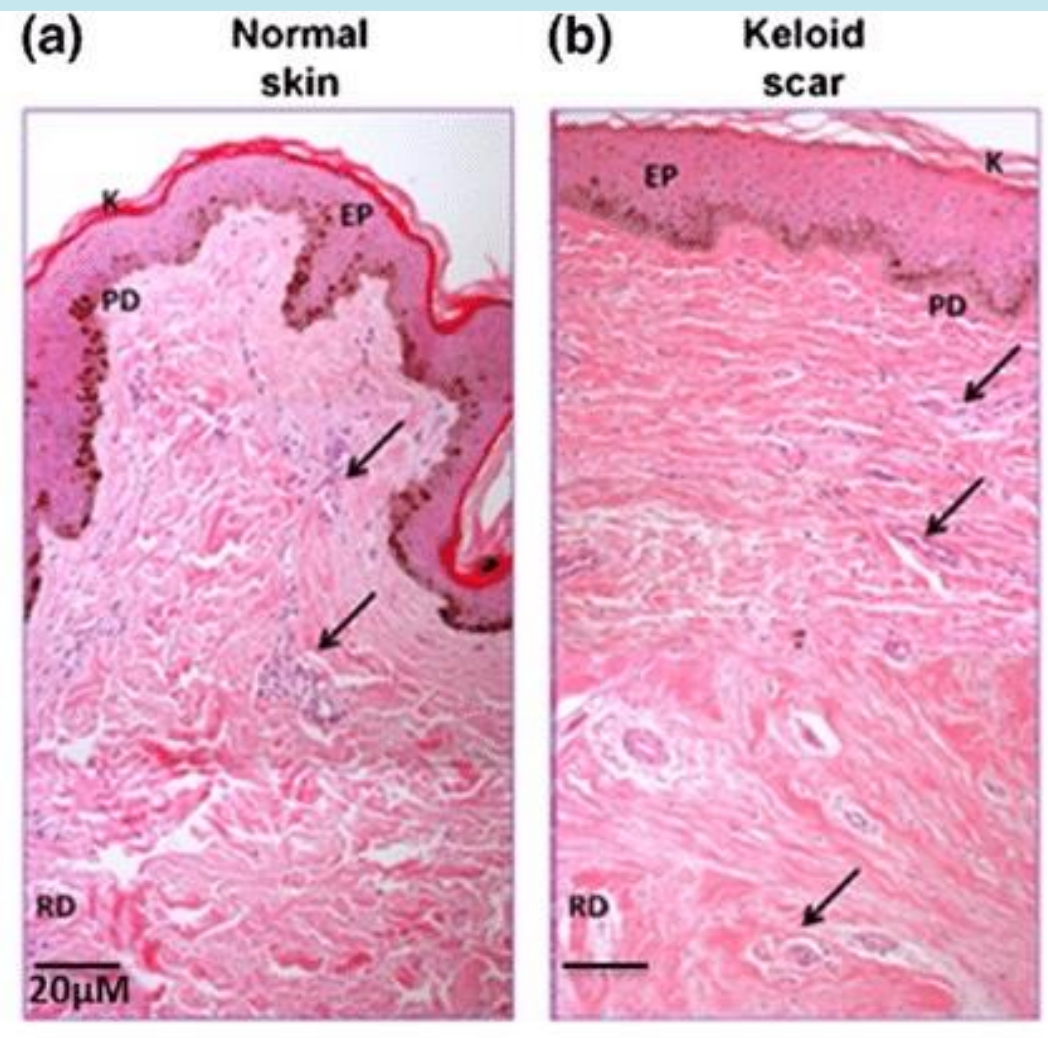


Figure 1. Normal skin vs keloid skin under microscope  
DOI:10.1007/s00403-014-1512-4

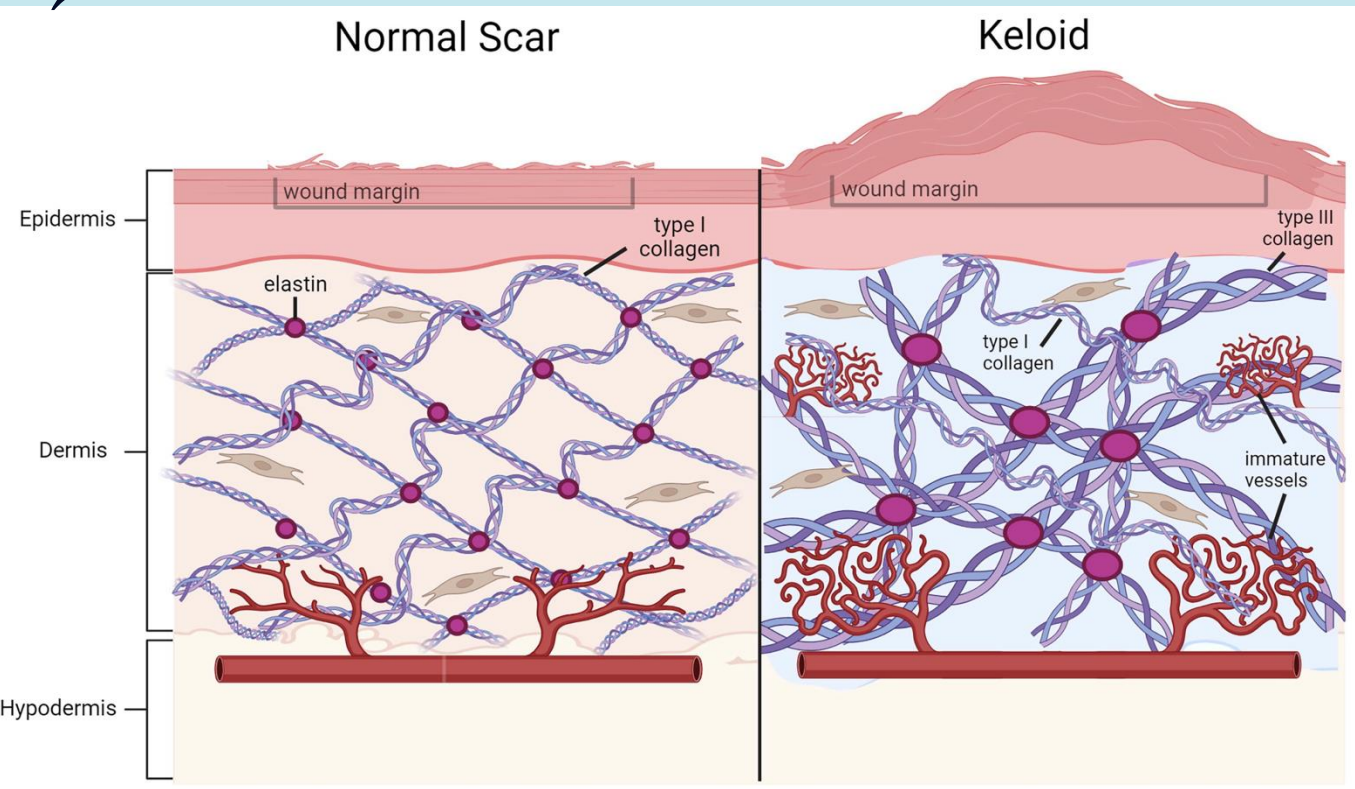


Figure 3. Diagram showing structural differences between normal scar tissue vs keloid from epidermis to hypodermis  
DOI: 10.1089/wound.2023.0185

| +ve association | -ve association |
|-----------------|-----------------|
| HLA-DRB1*15     | HLA-DQA1*0501   |
| HLA-DQA1*0104   | HLA-DQB1*0201   |
| HLA-DQB1*0501   | HLA-DQB1*0402   |
| HLA-DQB1*0503   |                 |

Figure 2. this table shows the statistically significant associations between the HLA alleles and keloid development

## RESULTS: FIBROIDS

- A **negative association** between **HLA-DOB** and **fibroid risk** was found.
- Serum HLA-G levels studied, but in comparison to other gynaecological conditions.
- No other associations** found between HLA haplotypes and fibroids.

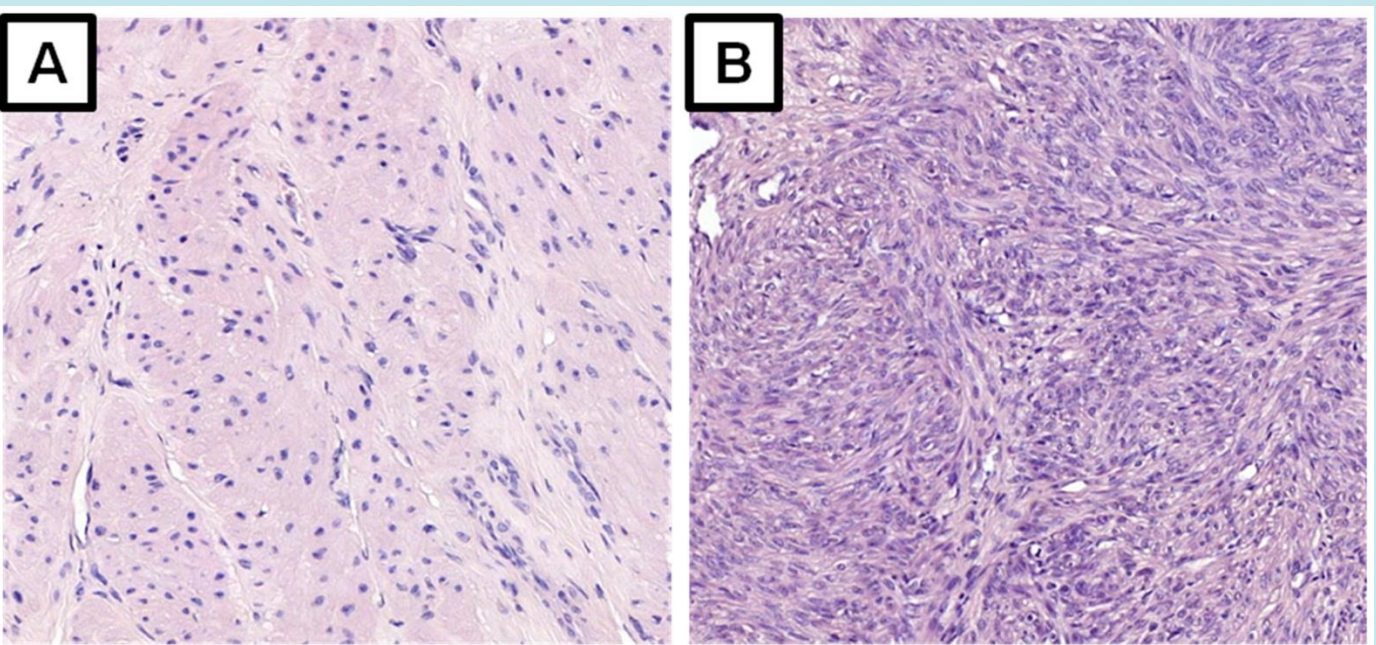


Figure 4. Microscopic slides, histologic specimens of the myometrium (A) and a uterine fibroid (B).  
Hematoxylin and eosin stain, 200× magnification.  
DOI: 10.3390/ijms19123869

## RESULTS: HYPERTENSION

Hypertensive individuals have more angiotensin AT1 receptor autoantibodies (AT1-AAs) contributing to arterial stiffening.

One study hypothesised that different HLA polymorphisms are associated with AT1-AA production. It found:

- HLA-DRB1\*04** associated with **increased** production of **AT1-AAs** — but is **not statistically significant**.

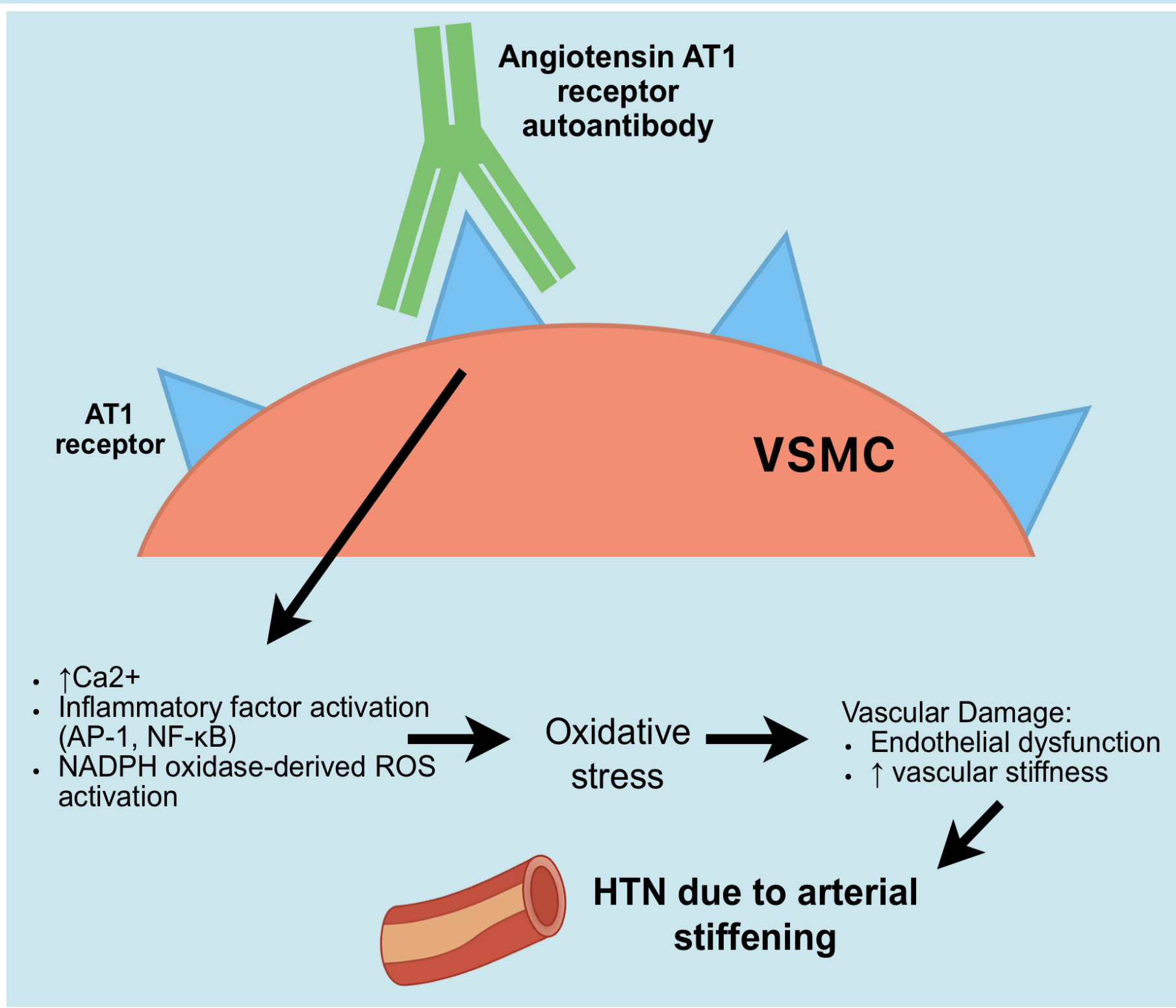


Figure 5. diagram showing the mechanism of action of AT1-AAs on the AT1 receptor

## CONCLUSIONS + FUTURE WORK

- HLA may contribute to **fibrosis in keloids and possibly hypertension**, but there is no consistent overlap across all three conditions.
- More multi-ethnic studies** are needed due to population-specific allele variability.
- There is potential for **screening high-risk individuals** using HLA markers, if validated. Literature suggests that hypertension could **aggravate keloid formation or recurrence**, indicating a possible **clinical interaction** worth further investigation.

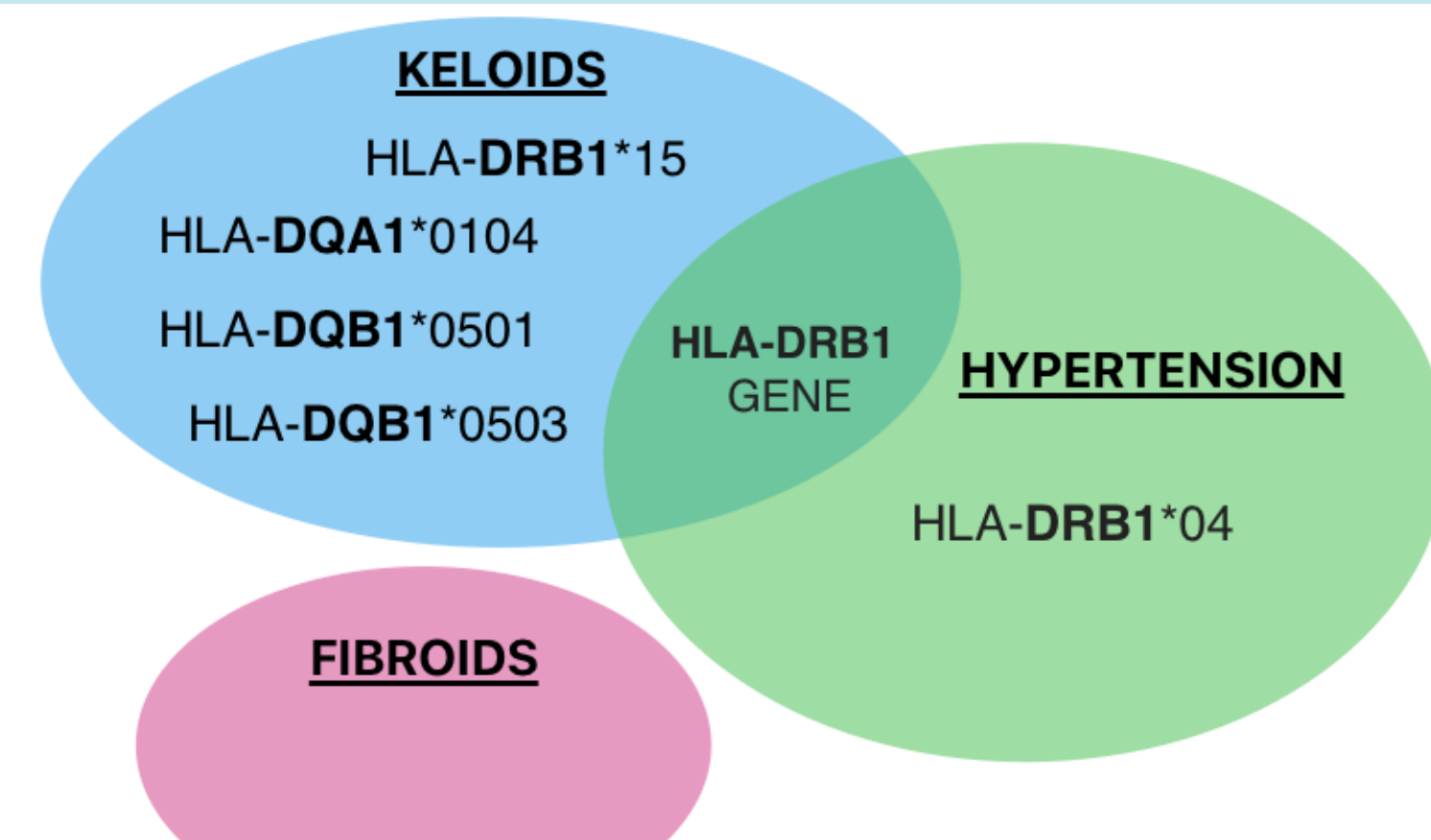


Figure 6. summary diagram showing relevant allele and gene positive associations for each condition