



Somatic PDGFRB Mutation in a Mosaic Aneurysm Patient

Dr. Ferreira Lab

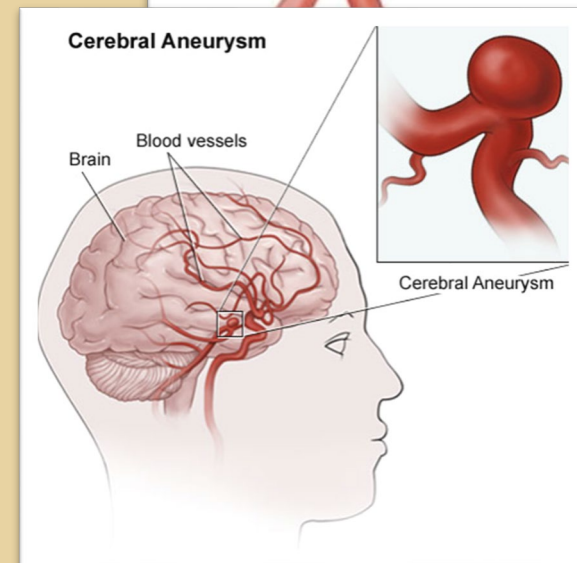
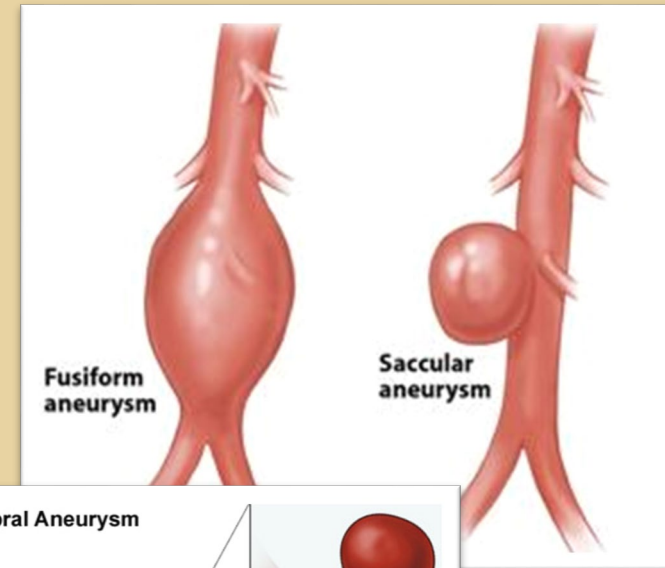
Daphne Toglia

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Background Information:

Intracranial Aneurysms

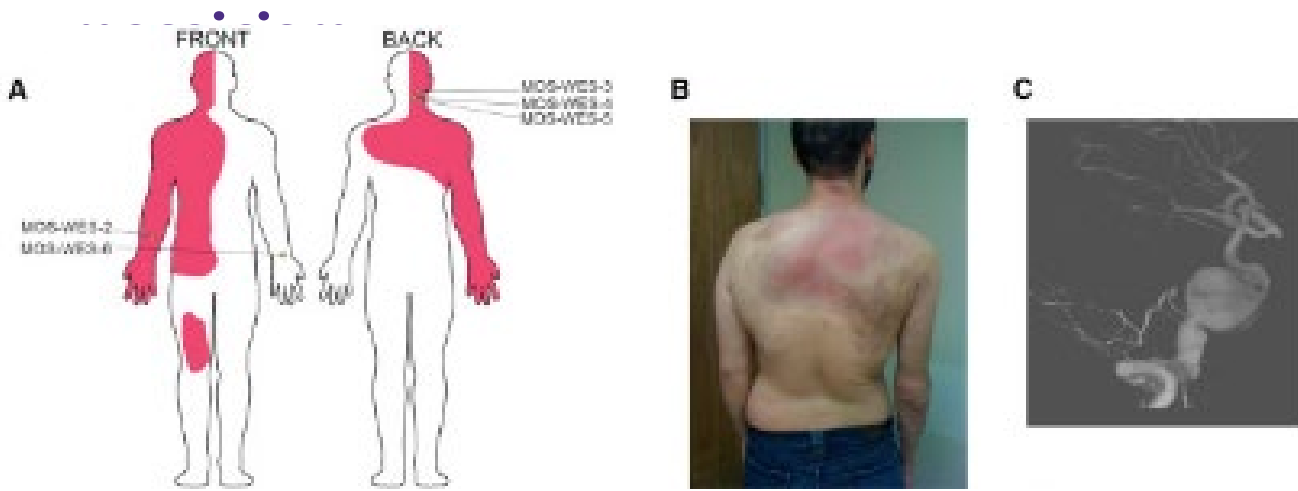
- > Intracranial aneurysms are relatively common, with a prevalence of approximately 4%.
- > There are two kinds of aneurysms, the more common saccular (90%-90%) and fusiform (4%-6%).
- > Abundant evidence supports a genetic component to the etiology of intracranial aneurysms.
- > The role of somatic genetic alterations or mosaicism in intracranial aneurysms remains unknown.
- > However, Dr. Ferreira's lab discovered that there is a somatic mutation involved.



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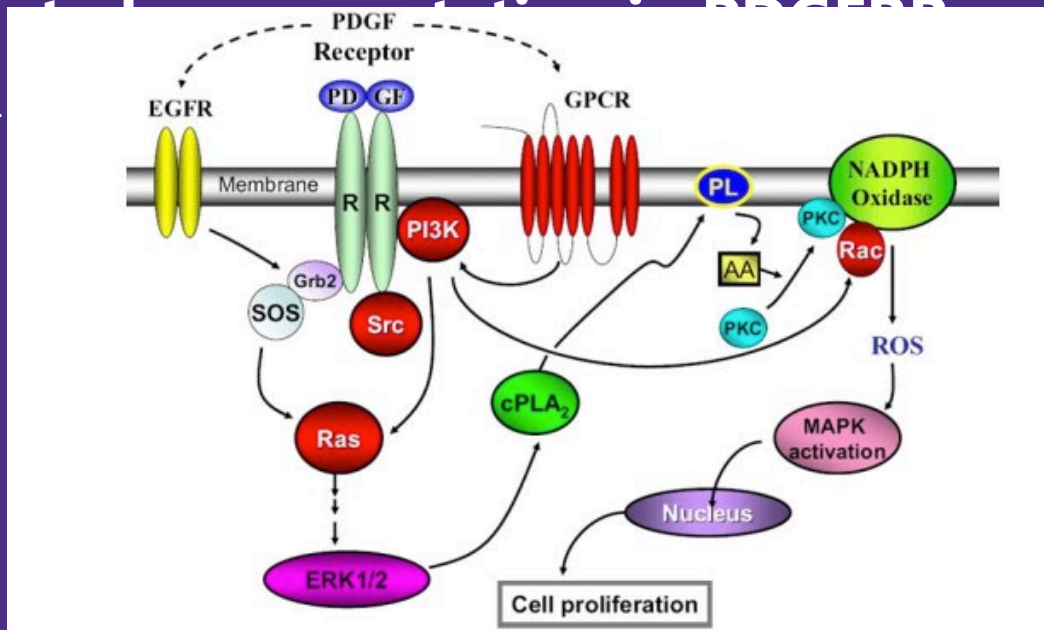
Background Information: Index Individual

- > A 22-year-old man presented at UWMC with progressive fusiform aneurysms on his right side.
- > The index individual underwent a series of genetic evaluations, but were unrevealing.
- > Genetic sequencing between blood and fibroblasts derived from the diseased areas detected a single novel variant predicted to cause a change within the platelet-derived growth factor receptor β gene (*PDGFRB*).
- > Notably, *PDGFRB* variant was not found in DNA isolated from blood or the histologically normal, left-sided, radial artery, therefore confirming post-zygotic or somatic



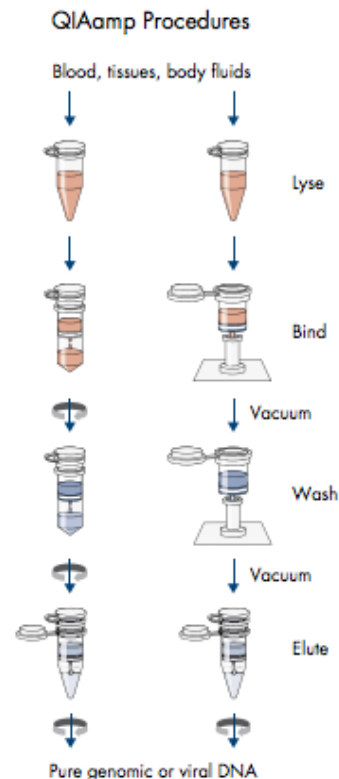
Background Information: Platelet Derived Growth Factor Beta (PDGFRB)

- > Activation of the PDGFRB receptor leads to the upregulation of downstream signaling pathways, most notably angiogenesis.
- > PDGFRB is normally expressed in several vascular cell types.
- > 4/6 fusiform aneurysm UWMC patients were also found to have increased PDGFRB expression.
- > PDGFRB is also found in saccular aneurysms



Methods: DNA Extraction

- > Process by which DNA is separated from proteins, membranes, and other cellular material contained in the cell/tissue from which it is recovered.
- > There are four commonly used DNA extraction protocols.
- > Dr. Ferreira's lab implements a solid phase extraction method.
- > Specifically, Qiagen QIAamp



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Methods: ddPCR

- > **Droplet Digital PCR (ddPCR)** is a method for performing digital PCR that is based on water-oil emulsion droplet technology.
- > A sample is fractionated into 20,000 droplets and PCR amplification of the template molecules occurs in each individual droplet.
- > ddPCR is capable of detecting low-level mutations using low nucleic acid inputs.



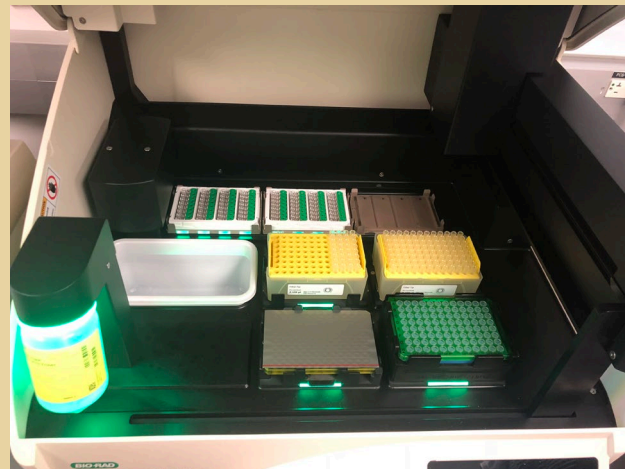
One measurement



Nanodroplet PCR reactions
are independent, single
amplification events

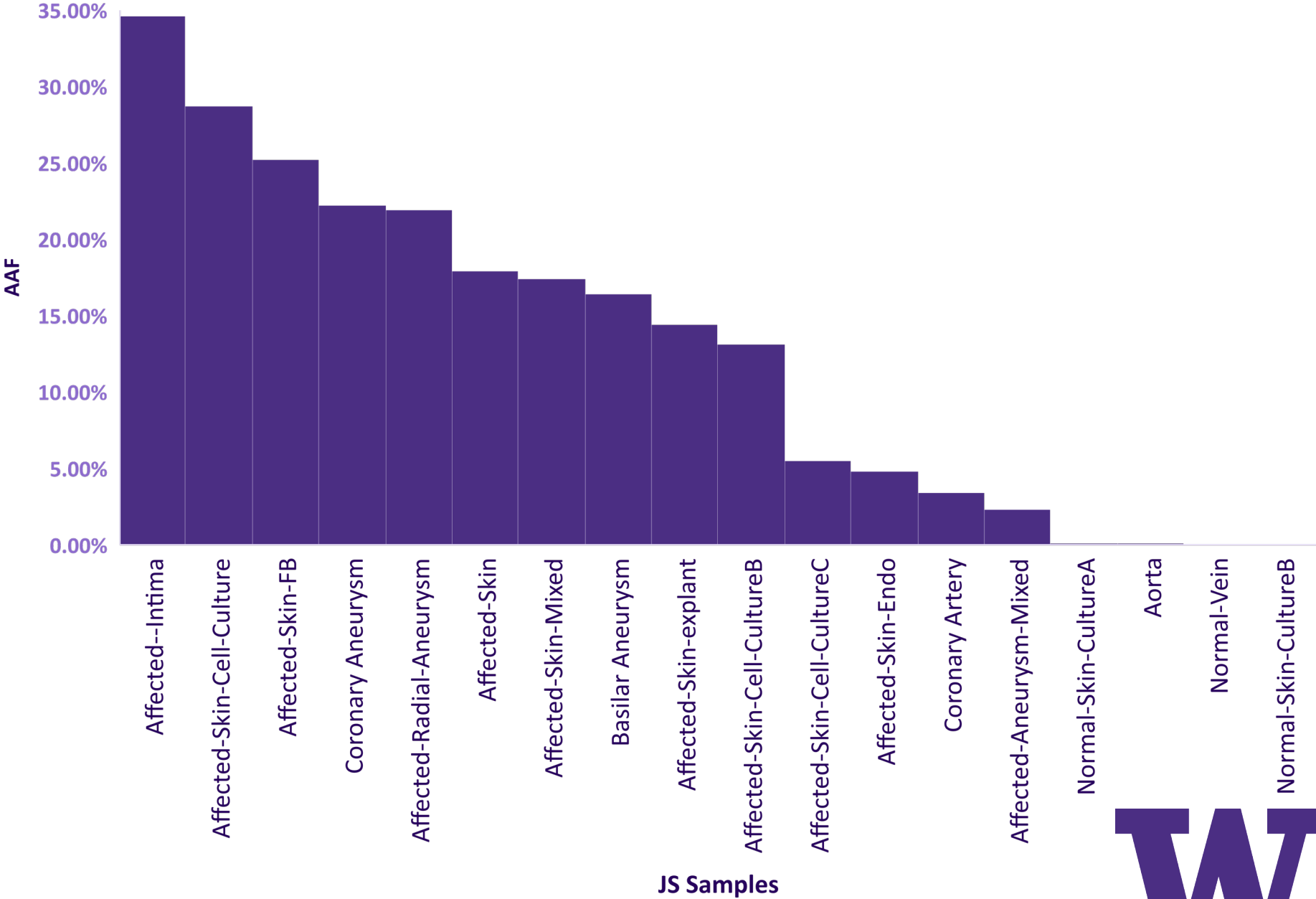


Many thousands
of discrete measurements

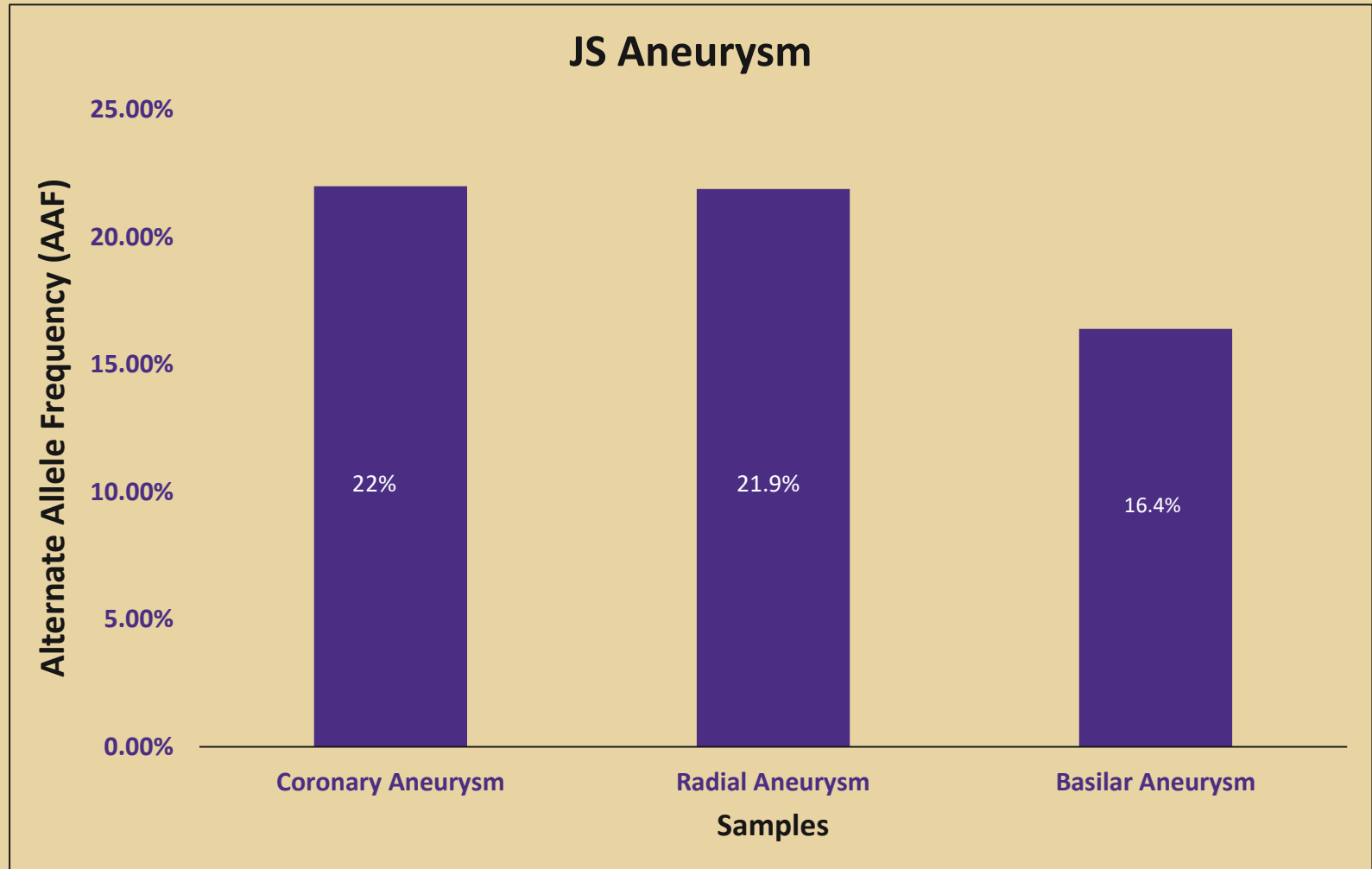


Findings

% Alternate Allele Frequency (AAF) of JS Samples



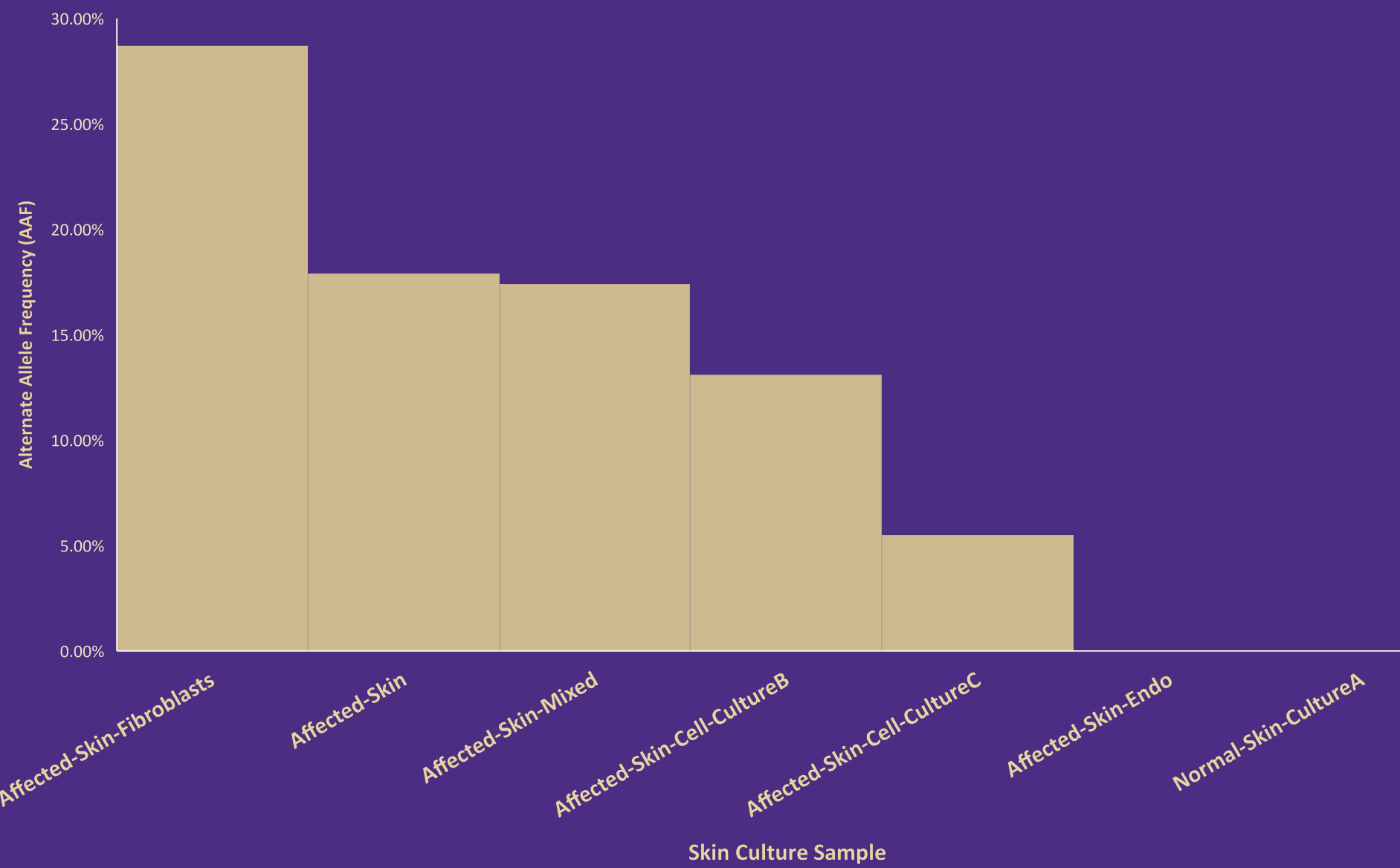
Findings



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Findings

JS Affected Skin and Skin Culture



Rest In Peace J.S

Conclusion/ Future Directions

- > Samples remain to be run through ddPCR and further analyzed.**
- > A larger cohort of cerebral fusiform aneurysm patients.**
- > Treatments and observing their efficacy remain.**
- > In conclusion, JS affected areas carry varying allele frequencies and cell of origin could be fibroblasts.**



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