A cheek smear to prevent sudden death

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Background

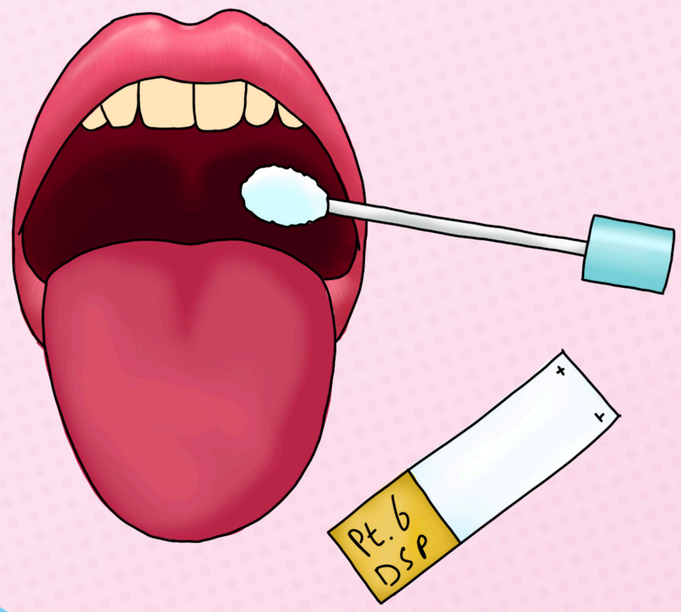
Every day in the UK, 12 people under the age of 30 die suddenly from a heart disease they did not know they had. Arrhythmogenic cardiomyopathy (ACM) accounts for >10% of sudden cardiac deaths (SCDs) in the paediatric population.

ACM is primarily caused by DNA mistakes that affect desmosomes: structures responsible for cell-to-cell adhesion. Our previous work has shown that the distribution of desmosomal, signalling, and junctional proteins is irregular in the hearts of patients with ACM. However, this finding has limited use in living patients due to the need for a heart sample. We have managed to circumvent this obstacle by showing that the same protein shifts occurring in the heart, also occur in the inside of the cheek.

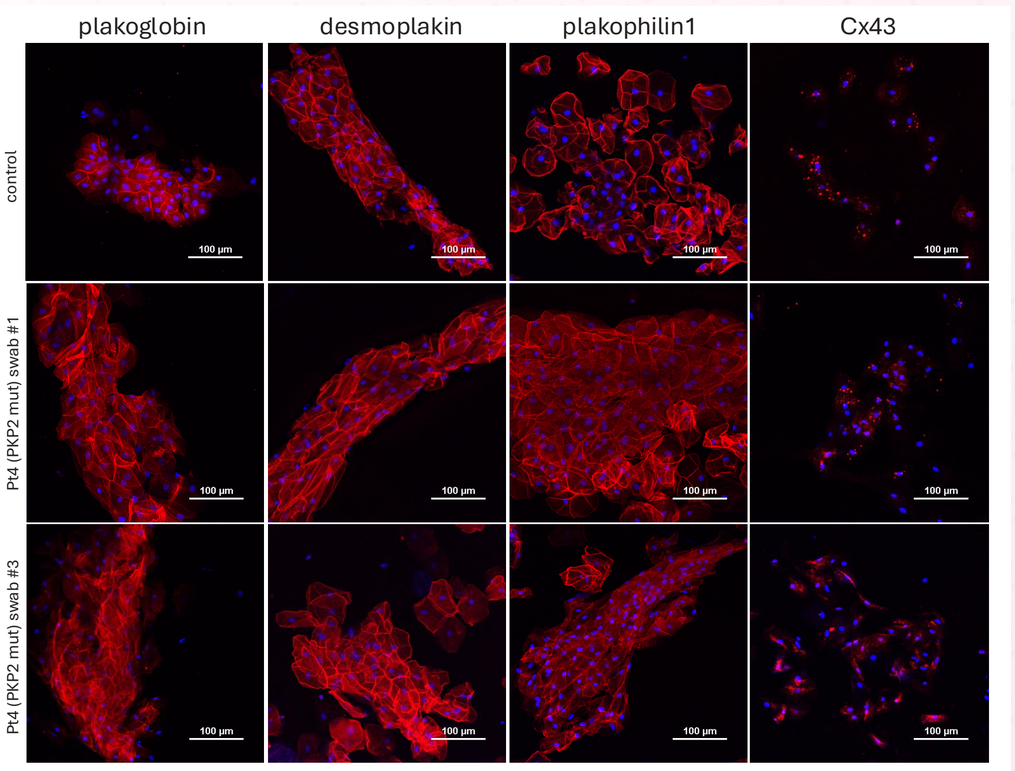
What did we do?

We collected buccal smears (cheek swabs) every 3-6 months from children who have been diagnosed with ACM, and children who carry an ACM-causing mutation but are not yet showing any evidence of disease.

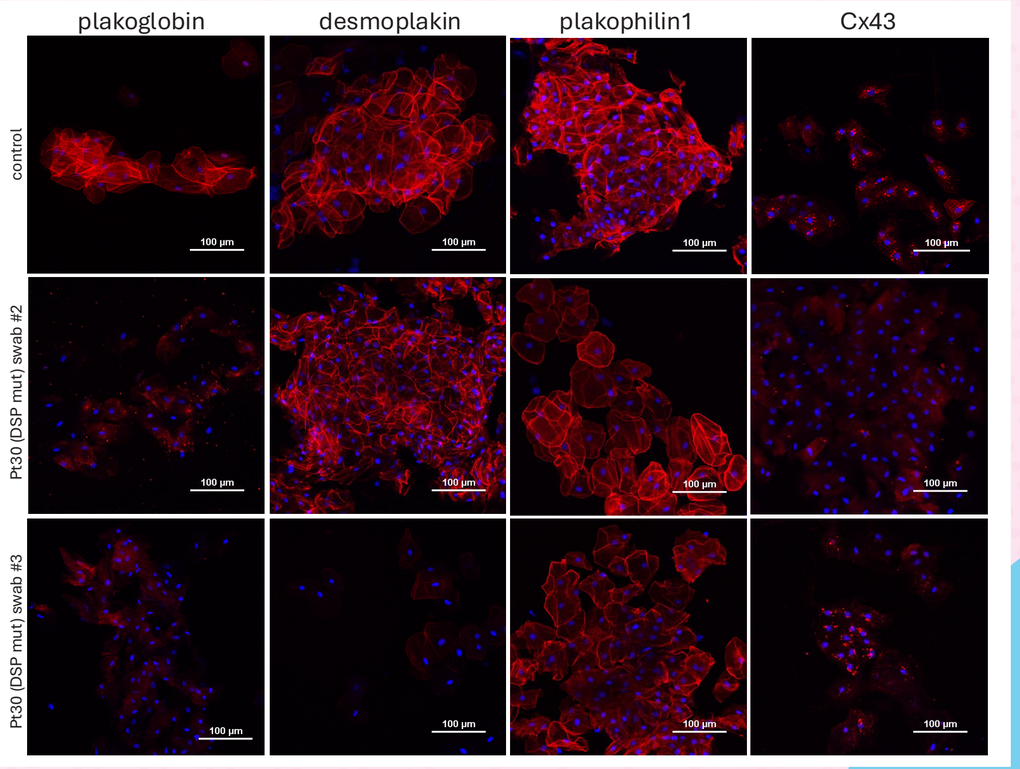
Buccal smears were subjected to immunocytochemistry for the desmosomal proteins plakoglobin, desmoplakin, and plakophilin-1, as well as the gap junction protein Connexin43, and the inflammatory protein RelA. Stained smears were imaged using confocal microscopy.



A



B, C



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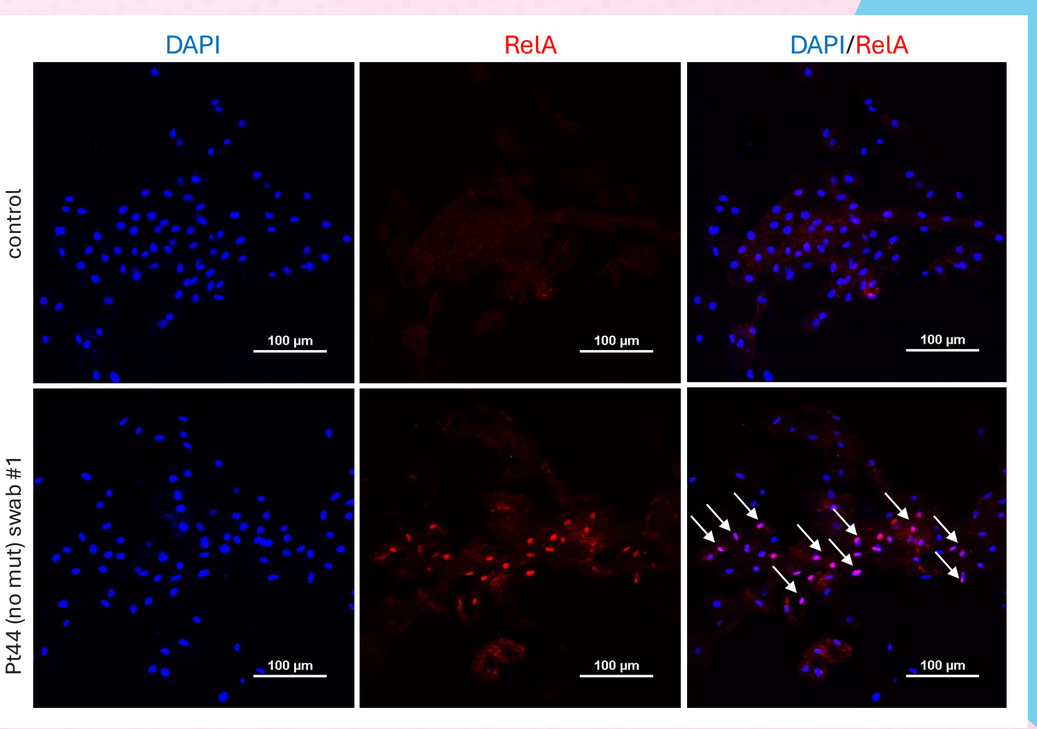

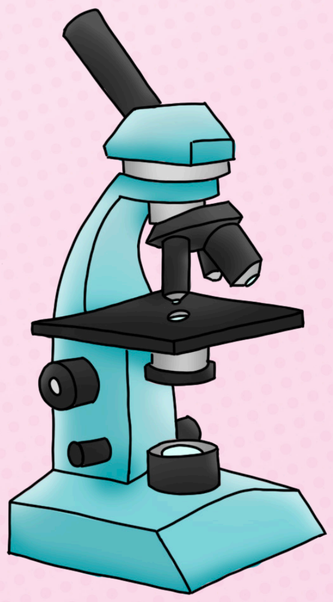

What did we find?

A – Although patients are born with DNA mistakes, proteins in the heart and cheek are normal at birth

B – Proteins start shifting before ACM manifests, while additional proteins shift as ACM progresses

C – Levels of Cx43 can be restored by effective anti-arrhythmic mediation

D – Inflammatory markers can predict when ACM patients will undergo a period of unstable disease activity (hot phase)

How does this work make a difference?

By adopting this safe, inexpensive, non-invasive, and risk-free method, for the first time we can detect ACM before the onset of disease fulfilling an urgent, unmet clinical need.

This novel tool has the power to significantly reduce costs and the burden on the NHS, and ultimately save lives

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