Genetic Diagnosis of the Rare Skin Disorder Pachyonychia Congenita

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Objective

- To confirm the clinical diagnosis of pachyonychia congenita (PC) by genetic testing.

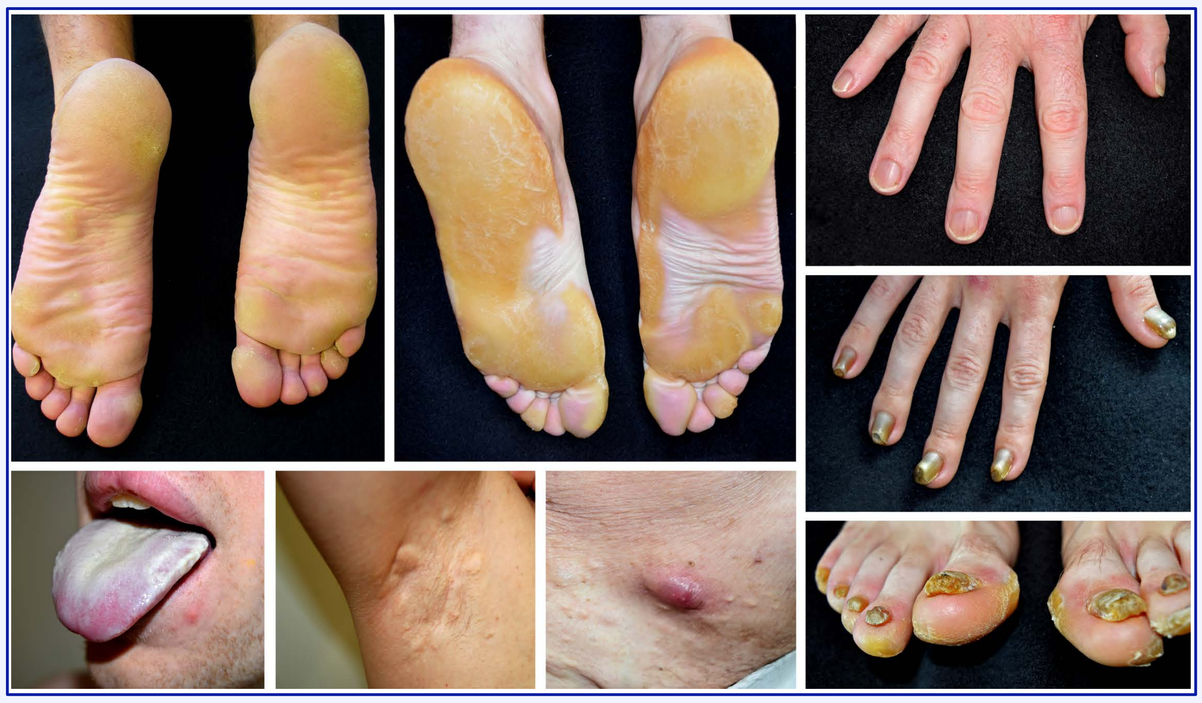
Methods

- The International Pachyonychia Congenita Research Registry (IPCRR), established by PC Project in 2004, collects clinical and molecular data from PC patients worldwide.
- Clinical consultations (by telephone) are performed by expert dermatologists combined with free genetic testing (University of Dundee).

Results

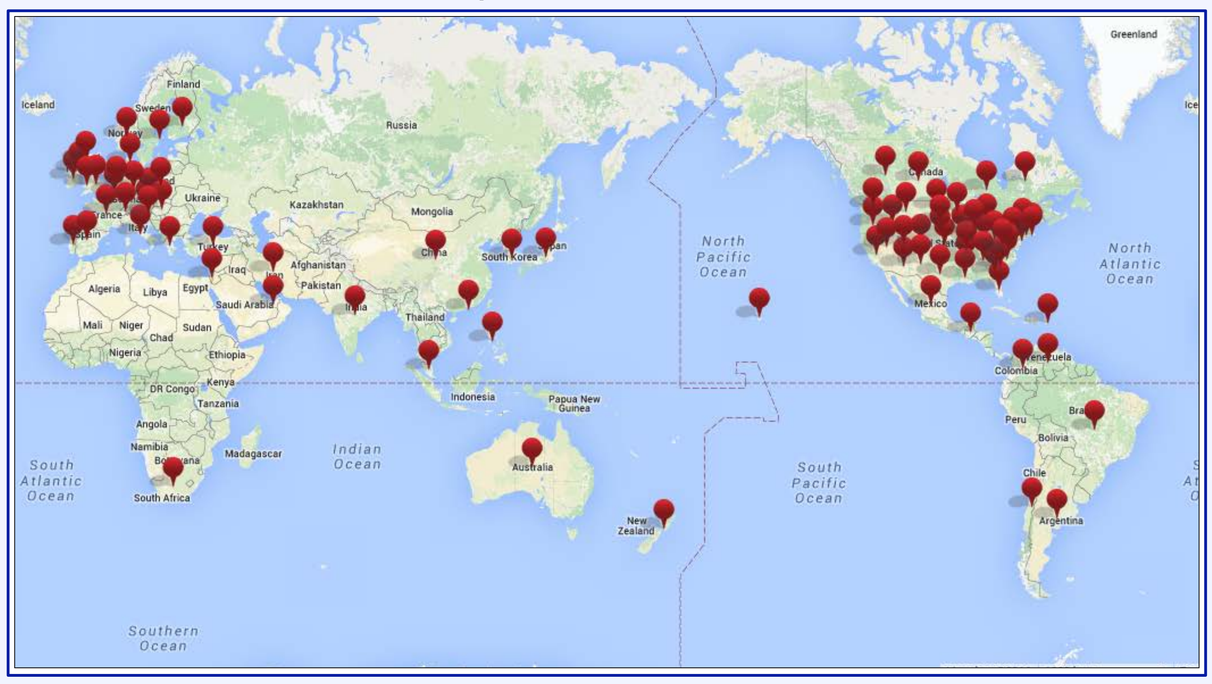
- PC is a rare autosomal dominant skin disorder.
- Characterised by severe plantar pain, palmoplantar keratoderma including calluses with underlying blisters, and variable hypertrophic nail dystrophy.
- Often there is oral leukokeratosis, cysts, follicular hyperkeratosis, palmoplantar hyperhidrosis and sometimes natal teeth.

Clinical features of PC



- The IPCRR has collected data from nearly 700 PC patients.

Location of PC patients with confirmed PC

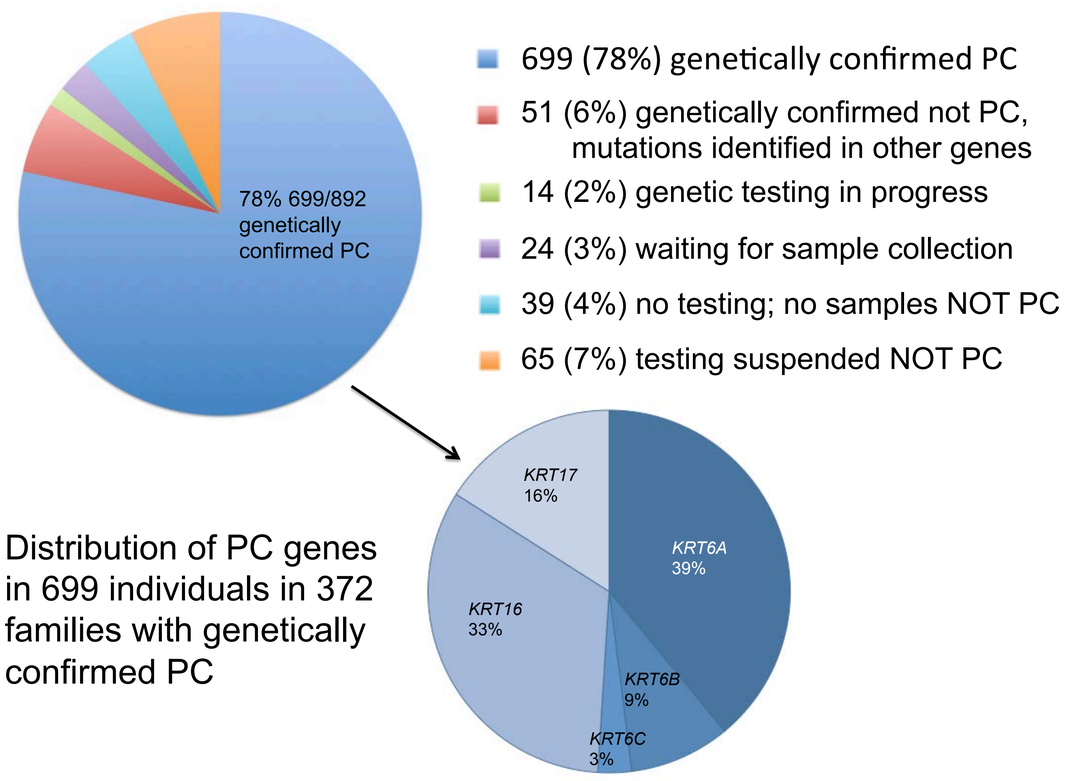


Results

- The underlying genetic cause is a mutation in any one of five keratin genes, *KRT6A, KRT6B, KRT6C, KRT16* or *KRT17*.
- More than 100 different mutations have been identified.
- The majority are heterozygous missense mutations.
- Genetic diagnosis confirms a clinical diagnosis allowing appropriate care and genetic counseling.
- The system is very accessible as patients can self refer through the website or via a clinician referral.
- Through this expanding database of molecular and clinical data it became apparent the historical nomenclature of PC was out dated; this has since been revised making it easier for clinicians and patients.
- An equally important service through the IPCRR has been the exclusion of keratin gene mutations from a small number of misdiagnosed patients, confirming they do not have PC.
- In some cases we have provided a correct diagnosis by identifying mutations in genes including *GJB6, TRPV3, DSG1*, *DSP* or *FZD6*, which present with some features of PC.

IPCRR status report – Apr 2016

892 individuals in 543 families



Distribution of PC genes in 699 individuals in 372 families with genetically confirmed PC

Conclusion

- Currently there are no specific treatments for PC but a correct diagnosis is the first step towards this goal.
- The wealth of data, clinical and molecular, that continues to be collected by the IPCRR not only ensures correct diagnosis for patients but is driving the development of future treatment studies.

References

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Acknowledgements

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