# Ectodermal Dysplasia and WNT10A

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As we know, Ectodermal Dysplasia (ED) comes in all shapes and sizes, with a search through the medical literature indicating over 150 possible different conditions. For many years, the cause of these various forms of ED remained a mystery, although with recent advances in genetic medicine and DNA sequencing, we are now gradually beginning to understand the true nature of at least some types of ED.

By the start of 2016, the molecular basis of ED had been discovered in about a quarter of all the different types, but significantly these discoveries also included the more common forms of ED, such that it is possible to work out the genetic faults present in well over half of people living with ED.

One of the recent genetic discoveries includes a gene called *WNT10A* (pronounced WINT-TEN-AY, although its full name is wingless-type MMTV integration site family member 10A). So, what is WNT10A and what does it do? Well, it turns out that WNT10A is a rather important protein that acts as the conductor of an orchestra, directing several other proteins that play roles in constructing and maintaining numerous body tissues, particularly those from the ectoderm – such as skin, hair, nails, sweat glands, teeth, etc.

If a gene mutation occurs in *WNT10A*, then ectodermal development is no longer in tune, and the result is a form of ED. In fact, genetic abnormalities in *WNT10A* result in two forms of ED, neither straightforward to pronounce, called Schöpf–Schulz–Passarge syndrome (SSPS) and odonto-onycho-dermal dysplasia (OODD).

SSPS was first described in Germany in 1971 by Dr Erwin Schöpf, Dr Johann Schulz and Dr Eberhard Passarge. Clinically, SSPS is characterized by eyelid cysts (apocrine hidrocystomas), increased thickness of skin on palms and soles (palmoplantar keratoderma), missing teeth (hypodontia), excessive sweating (hyperhidrosis), loss or reduction of hair (hypotrichosis), and abnormal nails (onychodystrophy), sometimes with other ectodermal developmental anomalies. Many of the features only manifest or worsen during adulthood. This late appearance of problems means that SSPS can be difficult for physicians or geneticists to diagnose – some people may be in their 50's before the diagnostic penny drops.

OODD was first described by Dr. Mahmoud Fadhil and colleagues from Lebanon in 1983. OODD shows clinical overlap with SSPS, including abnormal nails and misshapen teeth, along with skin thickening of the palms and soles and variable sweating problems.

The main difference between SSPS and OODD appears to be the occurrence of eyelid cysts in SSPS, although analysis of the specific changes in the *WNT10A* gene has shown identical findings in some cases of both conditions, and therefore SSPS and OODD might be considered as the same clinical entity. SSPS and OODD, even when taken together as a single form of ED, are rare with perhaps less than 100 people with this type of ED appearing in the medical literature.

## Supporting a normal lifestyle

The inheritance of SSPS and OODD is autosomal recessive. This means someone with the condition has to inherit two faulty copies of *WNT10A*, one from each parent. But what has become apparent is that some people who just have one abnormal copy of *WNT10A* can actually have some ectodermal abnormalities too – perhaps not enough to merit a diagnosis of ED, but nevertheless single mutation carriers can have changes in their hair, nails, teeth or sweating which demonstrate that even a conductor with one arm cannot keep the orchestra playing fully in the right key or with the correct tempo.

It is estimated that about 1 in every 200 people is a carrier for one faulty copy of *WNT10A* and that about half of these individuals will have clinical symptoms of signs of ectodermal anomalies. This means that about 1 in every 400 people in the world will have something wrong with part of their ectoderm – often hair or nails for females, teeth for males (although this varies a lot). So, the reality is that far from *WNT10A* only being relevant to a few people with rare forms of ED, it is in fact part of the daily lives of millions of people across the world, although most will have no idea that *WNT10A* is responsible.

At the moment, there is no treatment available to correct the primary *WNT10A* conducting problem, although in the future it is hoped that recombinant protein therapy (as for ectodysplasin) might enter clinical trials. That said, however, it is clear that WNT10A signalling in the body is extremely complex and being able to restore exactly the right tune for a healthy ectoderm may not be straightforward. For people living with SSPS or OODD, as with most other forms of ED, the best clinical care should be focused on treating troublesome symptoms through medical practitioners and other healthcare personnel.

## Supporting a normal lifestyle