

# European effort for the improved diagnostics of rare primary immunodeficiency disorders.

Anna Berglöf, A. Charlotta Asplund, C.I. Edvard Smith, Karolinska Institutet, Stockholm, Sweden



The revolution in molecular techniques over the last decades has paved the way for definitive genetic diagnosis of a very large number of disorders. This is particularly true for monogenic diseases. There are 150 different rare primary immunodeficiency disorders (PIDs) for which the molecular basis has been defined, thus enabling definitive diagnosis. In a collaborative European approach we combine different tools of genomic analysis in order to develop high-throughput diagnostics of PIDs.

## SUMMARY

We are developing innovative, high-throughput technologies for diagnosing genetic disease in individual patients. The main emphasis is on massive, parallel DNA sequencing, which allows the simultaneous analysis of very large numbers of genes, perhaps even all PID genes (currently around 150) in a single run. This will result in that the diagnosis will be made much more quickly and at reduced costs. This will offer improved patient care through early diagnosis, patient classification and improved risk profiling. Moreover, many of the strategies and techniques, when fully developed, can be used in different disease-areas and benefit patients having other forms of genetic diseases.

The project is granted by the EC within FP7:  
HEALTH-F5-2008-223293  
January 1<sup>st</sup> 2009 - December 31<sup>st</sup> 2011

## PROJECT PARTNERS

Karolinska Institutet, Stockholm, Sweden  
University College of London, UK  
GATC Biotech AG, Constance, Germany  
Children's Memorial Health Institute, Warsaw, Poland  
Uppsala University, Uppsala, Sweden

## THE NEED FOR PROPER DIAGNOSIS

PIDs are rare, chronic diseases. The hallmark of PIDs is increased susceptibility to infections. However, in certain PIDs the frequency of tumours is significantly enhanced and, in some forms, severe autoimmune phenomena predominate. Heterogeneous clinical presentation and/or locus heterogeneity is common. This also means that *making correct diagnosis is highly complex*. Thus, the symptoms and signs presented by a patient may not be typical for a particular disease entity, and even when they are typical, there are frequently a number of genes, which could cause a similar disease when mutated. Moreover, for many diseases there are genotype-phenotype correlations, meaning that symptoms and signs are influenced by the location and type of mutation.

## IMPORTANCE

The majority of PIDs give symptoms already during the first months/years of life. An important reason for developing efficient mutation detection is that early diagnosis is key for the treatment of these severe disorders. It is highly important to begin treatment at an early age, since patients may otherwise succumb to infections or other disease phenomena.



Karolinska Institutet  
Anna Berglöf, VMD, PhD  
Clinical Research Center  
Dept of Laboratory Medicine  
Hälsövägen 7  
SE- 141 57 Huddinge, SWEDEN

E-post: [anna.berglof@ki.se](mailto:anna.berglof@ki.se)  
Telefon: +46-8-585 838 73  
Fax: +46-8-585 836 50  
[www.ki.se](http://www.ki.se)



**Karolinska  
Institutet**