from 2005 to 2008. It is the successor and an extension of EUROGLYCAN, a network that was created in 1999, and funded under the Fifth Framework from 2000 to 2003, as a Research and Technological Development (RTD) project. European laboratories were in a particularly good position to provide a major impetus to this research, because these diseases were first identified in Europe. As a result of this collaboration, most new cases and types of CDG have also been identified in Europe.

The CA is meant to integrate research. The funding is essentially limited to coordination and integration via meetings, training courses and other types of exchanges, and in this case, also to the expert diagnostics and eventually the therapeutic trials. The network relies on other grants for the more fundamental research activities.

The challenge for this network is to keep up with the growing list of diseases in this area, and to warrant early diagnosis for this plethora of diseases. From a research standpoint, it would be interesting to see what the role of glycosylation and glycosylation defects is in the more common diseases like diabetes and neurodegenerative disorders. However, the major challenge for the (larger) clinical and basic research community will be to develop therapies for these complex diseases. One wonders for instance whether enzyme replacement would have a role in their treatment, or whether simple, pharmacological agents could be identified to bypass the deficient enzymes or boost their activity.

The merit of this network is that, within a few years, it has consolidated the European lead on clinical and fundamental research into these diseases. At the same time, it has shown that for rare diseases, the close interaction between expert clinicians and specialised researchers, together with the centrally monitored 'carousel' testing, are the key to success. This network could stand as a model for the organisation and integration of clinical and basic research for other rare diseases, in and beyond the metabolic field.

Clinicians who wish to share patient material with the network can either contact the network or the national referral centres, via www.euroglycanet.org. The network of course also accepts samples from abroad. Research groups or companies that are interested in contributing to the research in this field are invited to contact the coordinator■

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Cascade Screening

Whose information is it anyway?

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Cascade screening, that is, systematically approaching relatives of patients affected by genetic disorders, is controversial. Objections include that it undermines the autonomy of relatives, as they may be (or at least feel) pressurized to participate in the program, and that it is an invasion of their privacy, more in particular their right '*not* to know' that they are at risk. The validity of these objections is questionable. Firstly, much will depend upon *how* relatives are approached and informed: is the approach coercive or not, is the information provided stepwise, do people get time to think through the issues involved, etc.[1] It is important to spell out the primary aim of a cascade screening program. Is it to contact and inform as many relatives as possible in order to enable them to make informed decisions regarding testing and possible preventive measures? Or does the program aim at testing all relatives at risk? In the latter case, the program would be at odds with the requirement of voluntary participation in the screening. Secondly, critics tend to ignore that relatives may have the right *to know,* conditional upon the preventive value of the information. An ethical view that focuses exclusively on relatives' right not to know does not do justice to the (possible) relatives' health and/or reproductive interests involved – and is, therefore, one dimensional. Thirdly, in traditional clinical genetics, the professional standard urges counselors to explicitly point to the possible interests of clients' relatives – 'the patient is the family'. If one accepts this practice, one cannot consistently argue that cascade screening

is *a priori* unjustified. Clinical geneticists who object to cascade screening may of course argue that lack of time and personnel make it difficult for their center to engage in cascade screening. It is important, however, not to confuse such practical and logistic problems with ethical objections.

Clearly, the attitudes and experiences of relatives are highly relevant. In their interesting article in this issue, Newson and Humphries present an overview of previous cascade screening programs, directed at familial hypercholesterolemia (FH), cystic fibrosis (CF), Duchenne muscular dystrophy (DMD), and alpha-1 anti-trypsin deficiency.[2] Cascade screening was well-accepted by a large majority of the relatives involved. Partly in view of this positive experience, it was recently decided to intensify cascade screening for FH in The Netherlands. Cascade screening has also been performed to contact relatives at risk of carrying fragile-X-syndrome.[3,4] In The Netherlands, patient organizations strongly support this active approach.[1]

In view of both these normative aspects and empirical data, the real question is not *whether* cascade screening can be morally justified but *on what conditions*.

Newson and Humphries focus on one ethically contentious aspect of cascade screening, namely the methods by which relatives can be contacted. 'Family contact' or proband-initiated contact represents the standard practice in clinical genetics. In order to answer the question whether *direct* contact by professionals is justified, they provide a systematic account of its 'pros and cons'. The wording of their main conclusion is somewhat ambiguous; while the abstract states that direct contact is ethically justified, they conclude their article in a more differentiated way: rather than straightforwardly and inflexibly adopting the direct contact method, it is preferable to do this only after initial family contact has been established by the proband, if he indicates the wish to do so. This two-step approach seems to me a well-considered compromise, which does justice to all the complexities and intricacies of contacting relatives.

Various aspects need further scrutiny, including the following: Firstly, cascade screening, like population screening, can only be justified if it meets the principle of proportionality: the possible benefits should outweigh the possible harms. Newson and Humphries rightly suggest that FH cascade screening meets this criterium, as preventive measures can substantially reduce high risks of serious harm. This screening is, however, complicated by divergences between genotype and phenotype; some people with FH mutations do not have high cholesterol. While DNA-tests are routinely used in FH cascade screening in The Netherlands, biochemical screening for cholesterol may be preferable.[5] An alternative would be to decide about the screening test(s) to be used taking into account the risk profile of individual families. Secondly, what about doctors' responsibilities towards relatives at genetic risk? Following the adagium 'the patient is the family', some commentators argue in favor of a new paradigm which considers genetic information to be the *property of the family* – an example of so-called 'genetic exceptionalism'. This view insufficiently acknowledges the proband's right to confidentiality. At the same time, this right is not absolute. Decisions about the weight of this right can best be made case-by-case, using the criteria summarized by Newson and Humphries. It is important to clearly discern situations where informing relatives can be morally *justified* on the one hand and situations where it would be *morally obliged* on the other. A *general* moral duty to warn relatives about genetic risks is highly problematic, both theoretically and practically. In the case of FH, however, I would argue that professionals have a moral duty to try to inform relatives if the proband is unwilling to do so. Thirdly, it is generally accepted that the ideal of nondirectiveness is crucially important in the context of *reproductive* genetic counseling. In the context of counseling carriers of preventable/treatable conditions like FH, a more directive attitude of the doctor seems to be justified. To argue that giving unsolicited advice to stop smoking is unacceptable is absurd. And finally, what about the position of children in affected families? Screening of children for FH is controversial. While the target group of FH cascade screening in The Netherlands is defined as people at risk of at least 16 years of age, younger children are often tested at the request of the parents. There seems to be an international trend towards earlier testing, aiming at maximizing the preventive value of FH testing. A complicating factor, however, is the uncertainty about the long-term safety and effectiveness of statin treatment in children with FH.[6] How to define the best interests of the (incompetent) child and related responsibilities of both doctors and parents in view of this uncertainty? The future development of FH cascade screening depends on further research and debate on these and other issues■

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