

Patient information – Euro-MRX project

This document contains a printable version of the patient information on the Euro-MRX website (www.euomrx.com). It contains information which may be of interest to the families of patients with MRX.

A number of subjects are discussed below, which answer the following questions:

- [what is mental retardation?](#)
- [what is MRX?](#)
- [what is the Euro-MRX project?](#)
- [why is the EURO-MRX project being carried out?](#)
- [what can I do to help the EURO-MRX project?](#)
- [what are the research activities?](#)

You will also find a section with [links](#) to other websites related to mental retardation.

What is Mental Retardation?

Mental Retardation (MR) is a disorder with a wide variety of symptoms. It is characterized by an IQ of less than 70, and coincides with behavioural and/or adaptation problems in daily life.

Nothing is known about the causative factors of MR in a large part of the patient population. In 20-45% of the severe cases of MR, the cause of the disease is not known at all. This percentage increases to 80% for the moderate and mild cases.

Both genetic and environmental factors can play a role in those cases for which a cause can be determined. Environmental factors in these cases may be, among others: birth defects, infections and toxins.

The genetic factors can be divided into chromosomal and monogenic causes. Trisomy 21 is the most common chromosomal cause, while other forms of trisomy, monosomy and microdeletions can result in the development of (severe) MR.

Thanks to the enormous improvements in the fields of clinical genetics and molecular biology, the knowledge about monogenic disorders has greatly improved. Finding new genes and analysing their protein product gives us new insights in to how the brain develops and functions.

What is XLMR?

As far back as 1890, it was recognized that there are more men than women in institutions for the mentally handicapped. Studies carried out in the following years confirmed that men outnumber women by 20-30% when it comes to patients with MR. This led to the assumption that genes located on the X-chromosome play a major role in MR.

The first important evidence for this theory came in the 1970s, with the discovery of the Fragile X syndrome. Several other X-linked forms of MR were soon identified. These disorders all belong to the group of X-linked Mental Retardation (XLMR).

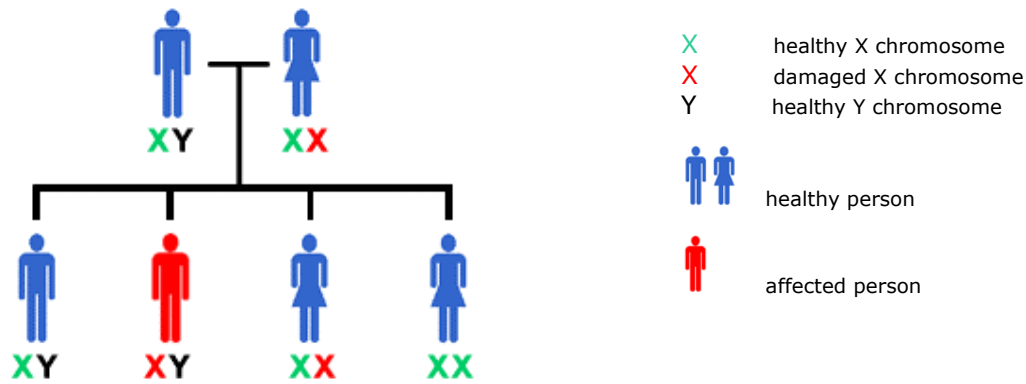


Figure 1: pedigree showing X-linked inheritance

Figure 1 shows how an X-linked disorder (XLMR in this case) is inherited within a family. The main characteristic of this type of inheritance is that only men are affected by the disorder. This is because men do not have a second (healthy) copy of the X-chromosome which can compensate for the damaged copy. Instead of a second X-chromosome, like in women, men have a Y chromosome. The Y chromosome can not compensate for a damaged X-chromosome, because their functions are largely dissimilar.

From the above follows that women are seldomly or never affected by an X-linked disorder. They can however be carriers of the disease, in which case the healthy X-chromosome can compensate sufficiently and leave the women in question unaffected. In very rare cases a woman can receive two damaged copies of the X-chromosome and develop the disorder.

Nowadays, XLMR is divided into two groups:

- Non-syndromal or non-specific XLMR, named MRX
- Syndromal XLMR, named MRXS

In MRX, the mental retardation is the only symptom of the disorder, without any neurological, metabolic or dysmorphic features.

The group of patients with MRX are the focus of our research. The identification of new genes involved in MRX has been particularly successful over the past few years. A total of 16 MRX genes are known today. The close cooperation of several research groups and the establishment of the Euro-MRX Consortium have played a major role in this success.

What is the EURO-MRX project?

The Euro-MRX Consortium is a cooperative organization of six institutes. These institutes have years of experience in research into the genetic background of mental retardation. Together with a number of associate research groups, the Consortium now puts all its effort into the EURO-MRX project.

The goal of this project is to identify new genes which play a role in the development of mental retardation, in addition to the 16 genes known to date. By investigating the biological function of these genes, we hope to accomplish the following:

- Increase the possibilities for DNA diagnostics on MRX
- Improve the support for patients and their families
- Increase the knowledge of the functioning of the human brain

The results of the research of the EURO-MRX project will be made available to patients and their families, by keeping in close contact with patient organizations and the like.

Why is the EURO-MRX project being carried out?

In only 50% of all patients affected by mental retardation (MR), a cause for the disorder can be identified. This percentage is kept low by the lack of good diagnostic tests for most forms of MR.

For X-linked MR (MRX) there are no diagnostic tests available at all. This keeps the cause of the disease unclear, while clarity is badly needed. Not just for the prognosis and treatment of the patient (which is all important in itself), but also for genetic counselling of family members involved.

The main goal of the EURO-MRX project is therefore to increase the possibilities for DNA diagnostics for MRX (to read about the other goals, please see the page Research Program on www.euomrx.com). We expect that our research will lead to at least twice as much diagnoses of MRX as are possible today.

What can I do to help the EURO-MRX project?

The research carried out by the EURO-MRX project is completely dependent on the availability of DNA material from patients with MRX. The more patients we can add to our activities, the bigger our chances are of finding new genes. And the bigger our chances of getting closer to understanding mental retardation.

We are looking for families in which MRX is (possibly) present. Such families always have several males affected by mental retardation (please also see the page What is XLMR?). You may be interested in helping us find possible candidates for our research.

Perhaps you know of a family with several males affected by MR, or maybe you are a member of such a family yourself. You could then help us by letting the people concerned know about our project and ask them if they are interested in participating (that is, giving blood for the creation of a cell line). The GP/physician will be able to determine whether a particular family may be suitable for referral to our project, and contact us if this is indeed the case.

Your help is very much appreciated!

Summary of research activities

There are an estimated 50 to 100 genes on the X-chromosome which are involved in MRX. Up till date, 16 of those genes have been identified. We want to discover exactly what role these 16 genes, and the ones yet to be identified, play in the development of MRX.

To this aim, the EURO-MRX has at its disposal DNA and pedigrees of over 240 families in which MRX is present. There are strong clues that the mental handicap in these families are caused by a defect in a gene or genes on the X-chromosome.

Mutation-analysis will be carried out on the DNA of the 350 MRX families. This method will show which genes are most frequently mutated. For 11 of the 16 known genes, this analysis has been carried out already. Also, a 100 candidate-genes have been tested on a part of the collection of families. This has resulted in the following findings:

- Almost all known MRX genes only make a small contribution to the development of MRX
- Many more families will have to be tested in order to discover the unknown genes

The genes which have tested positive in the mutation-analysis, will be further tested on a group of 500 patients. Of these 500 patients, the cause of their mental handicap is not known, but unlike the MRX families, they have no family history. If the tested gene is mutated often in the group of 500 patients, it may be suitable for use as a diagnostic test.

Up till now, mutation-analysis has revealed that two genes are more frequently mutated in the 240 MRX families than in the average population. However, this turned out not to be the case for the group of 500 patients, thus eliminating the genes as diagnostic candidates. Although this a somewhat disappointing result, publication of these findings ensure that no unnecessary diagnostic testing is done for these genes.

The role of all identified genes which play a role in MRX, the function will be determined by carrying out functional studies.

Links to other websites

On this page you will find links to other websites which have information about mental retardation and MRX. If you think a certain website should be added to this page, please feel free to email the link to links@euromrx.com.

www.thearc.org/faqs/mrqa.html

Clear and readable overview of scientific facts.

www.nichcy.org/pubs/factshe/fs8txt.htm

General patient information combined with scientific articles and a personal story.

www.aacap.org/publications/factsfam/retarded.htm

General introduction into mental retardation of the American Academy of Child and Adolescent Psychiatry.