Like the victims of other genetically-determined diseases, patients suffering from the hereditary polyneuropathies (e.g. Charcot-Marie-Tooth disorders or CMT) are face an almost total lack of therapies. A great many CMT4A patients are forced into wheelchair-use even at a still-young age. Furthermore, patients complain of sensation impairment. While agents made use of in treatment have known neurotoxic effects, medicine lacks knowledge of the potential neurotoxicity of drugs used to treat other disorders (e.g. lifestyle diseases) that may also affect CMT4A patients. It is equally possible that some of the well-characterised medical substances available on the market may exert a protective effect on the nerves damaged in CMT4A.

So far, the molecular pathogenesis involved in CMT4A disease is only known very selectively. It seems that recessive loss-of-function mutations lead to reduced mitochondrial fission activity. On the other hand, that the deliberate silencing of the *GDAP1* gene has been shown to lead to defects in a wide spectrum of processes, such as transport of mitochondria, the formation of contacts between a cell's endoplasmic reticulum and mitochondria, and calcium homeostasis. Since it is not even clear what the exact role of the GDAP1 protein is, it remains extremely difficult to assess which of these observed abnormalities are primary reasons for CMT4A, providing the main contribution to disease symptoms.

For many years now, our group has been diagnosing and consulting with many patients suffering from CMT4A disease, albeit caused by various different mutations in the *GDAP1* gene. This situation has allowed us to investigate the course of CMT4A disease very thoroughly, as well as to become acquainted with the numerous problems our patients face. It has also left us acutely aware of the urgency of effective therapy being implemented, in line with determinations as to which medicinal substances may prove inadvisable for this group of patients, only contributing to a further deterioration of an already-severe condition. By consulting with such an unique group of patients, we would like to investigate the modes of action of particular mutations. Beyond that, our ability to work with cells obtained directly from the patients will allow us to experiment on relevant genetic backgrounds, with the result that genetic manipulation is minimised, and the reliability of results increased in consequence. Detailed clinical and electrophysiological analysis of patients will help us assess the correlation between observed abnormalities at the cellular level and the course of the CMT4A disease. In our research, we are also plan to test a variety of commonly-used medical substances, to check how these improve or impair the cellular phenotypes observed in the case of each different mutation. For this purpose, we will be using a very well-known model organism in the shape of the yeast *Saccharomyces cerevisiae*, which has proved very effective in this type of screening. Preliminary data obtained in this way will then be confirmed using the cells from CMT4A patients.

We believe that an understanding of the mechanisms of action of selected substances will offer a basis for potential experimental treatment, and will draw our attention to those processes whose defects represent the main components of the disorder, and hence the main contributors to the development of CMT4A disease. It is thus our hope that our research may supply results that at least partially fill in the gaps in our basic knowledge of CMT4A disease, with the consequence that new therapies can be developed, and the quality of the lives of patients improved.