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The POF (Premature Ovarian Failure) syndrome is a secondary hypogonadotrophic amenorrhoea affecting about 1% of females younger than 40 years. In 30% of them POF is caused by genetic defects. In this dissertation the association between the POF candidate genes on the X chromosome and the pathogenesis of POF was investigated.

Firstly RT-PCR assays of a number of POF candidate genes in leukocytes were established. It showed that examination of DIAPH2, GPC3, E2F-f6, POF1b and BMP15 expression in the leukocyte is technical possible. Other candidate genes like HS6ST2, DACH2 and XPNPEP genes could not be examined because of their low transcriptional activities in blood cells. Based on single RT-PCR protocols two multiplex RT-PCR assays (DIAPH2/E2F-f6/POF1b and DBX/BMP15) were established. They showed that multiplex RT-PCR assays help make the POF genetic expression diagnostic more efficient but also present conditional limitations. After establishment of the RT-PCR assays the expressions of 4 POF candidate genes in leukocytes were investigated in 95 POF patients and 90 control females. It was found that the DIAPH2 and POF1b gene were expressed normally in the entire POF patient group. A grave genetic mutation which would cause loss of their expression could thus be excluded in these POF patients. POF54 has found with no expression of E2F-f6 in the leukocyte and this result needs to be scrutinised with an RNA sample from ovarian tissue. POF14 and POF123 showed no expression of GPC3. By the following genomic analyses large genomic deletions were excluded. 5´UTR or promoter defects suggested as putative causative agents. Promoter function analysis, like luciferase reporter assay would be helpful here for further clarification.

It can be shown in this thesis that RT-PCR assays in leukocytes for the study of expression of POF candidate genes can be seriously be taken as a first step in the molecular genetic diagnostic of the idiopathic POF syndrome. Its aim is to select a subgroup of POF patients with possible gene expression defects in the heterogeneous large idiopathic POF population.

Nevertheless, every result of the leukocyte gene expression assays needs to be scrutinized by an RNA sample in the ovarian tissue. With this diagnostic leukocyte expression assay the step of ovarian biopsy in the diagnostic of POF syndrome can thus be taken more effectively.

FMR1, its number of CGG-repeats in exon 1 and its methylation status was examined by ALF express fragment analysis and Southern blot. Four FMR1 premutation carriers POF99, POF101, POF118, and POF125 were found. The prevalence of premutation was estimated with 4.2% (95% CI [0.2%-7.9%]). It is higher than in the general female population with 0.4%. However, there is no association between the CGG repeat number and the FMR1 expression status.

Furthermore from to the results of the CGG repeat number analyses in the FMR1 gene and the methylation status of associated CpG island there were no association between the CpG island modification and mRNA expression level. It suggests that some other epigenetic regulation might play a role in the POF pathogenesis of these patients which needs to be explored by further research. It seems thus, that no only the CGG repeats number can influence the mRNA production of the FMR1 gene in leukocytes.