Introduction: Recurrent vulvovaginal candidiasis (RVVC) is diagnosed in females who suffer from three or more VVC episodes per year. As VVC is a non-recordable disease, there is no exact data concerning its incidence. However, it is estimated that approximately 5-8% of women of reproductive age are suffering from the recurrent form. Pregnancy is considered to be one of the predisposing factors for VVC. It is generally accepted, that RVVC has no significant influence on pregnancy outcome, however, this chronic disease has a major impact on the quality of life due to the recurrent symptoms. Concerning that many antifungal drugs are contraindicated in pregnancy it's even more important to develop new and more effective treatment modalities.

The disease is polygenic and multifactorial, in which apart from the pathogenic role of various Candida species, genetic, environmental and lifestyle factors are thought to be equally important. Fungal recognition of human cells is mediated via interaction of conserved pathogenic structures (PAMPs) on fungi cells interacting with pattern recognition receptors (PRR) on host cells. The result of these events is the modulation of the release of inflammatory mediators playing a key role in shaping the hosts' protective immune responses in order to eradicate the fungal burden.

The aims of this project are to identify and study the role of genetic factors playing a role in the pathogenesis of RVVC, and to develop new treatment modalities.

Materials and methods: Single nucleotide polymorphisms (SNPs) of candidate genes that are important for the molecular pathogenesis of the disease are analyzed from the genomic DNA obtained from the peripheral blood sample of 300 female volunteers. The control group consists of women at fertile age suffering from bacterial vaginosis.

SNPs of the dectin-1 (DECT-1) receptor that recognize the Candida cells, and CARD9, an important adaptor molecule playing a role in the intracellular signaling events leading to the initiation of immune events are studied in case-control studies by direct sequencing. Participants are also invited to answer a questionnaire concerning their socio-economic background and lifestyle in order to evaluate the contribution of various factors to the pathogenesis of RVVC.

Parallel with the genetic studies, in vitro testing of the pH sensitive release of different antifungal nanoparticles, and their effect on different Candida species is currently being investigated in order to develop novel treatment modalities.

Results: Over 20 potentially polymorphic nucleotides in case of the DECT-1 and more than 50 in CARD9 are currently being studied, judged by the available data found in various SNP databases. According to our results, the majority of these SNPs are either rare or they are not polymorphic in the Hungarian population. At least 2 SNPs in case of both genes that are indeed polymorphic are also identified. Currently we are comparing the distribution of various genotypes at these positions in controls and RVVC patients to find out if any of the alleles are playing a role in the genetic predisposition to the disease.
Discussion: Our results may enhance our current understanding of a chronic disease affecting a reasonable proportion of the female population, furthermore, it may also allows the design of more effective and well-tolerated targeted treatment modalities that can reduce or mitigate the effects of microbial vaginal inflammation often associated with decreased fertility and elevated incidence of premature birth in the Hungarian population. The newly developed nanocomposites, exhibiting a pH sensitive targeted release of antifungal drugs may help us to decrease the dose of the applied active components, and parallel to that, decrease the occurrence of side effects. Also, by improving the efficacy of the available treatments modalities we may also reduce the rate of recurrent fungal infections of the female population.