6. Summary

Dilated cardiomyopathy (DCM) is a heart muscle disease characterised by impaired dilation and contraction of the left ventricle or both (Richardson, 1995). Twenty percent of DCM belongs to the familiar/genetic form, the rest may be idiopathic, viral, auto-immune or immune-mediated associated with a viral infection (Caforio *et al*., 2002). The present work is divided into two parts. The first part shows the screening of phage antibodies to allow verification of previously identified targets. The following part of the work combines an expression library with protein array technology to identify new putative disease relevant auto-antigens.

First, antibodies were selected against differential expressed genes of DCM patients using phage display. 27 genes were cloned in an expression vector, followed by successful expression and purification of twelve of these genes. Phage antibodies against six of these recombinant expressed gene products have been selected. The incubation of these phage antibodies against protein extracts from mouse shows high cross reactivity.

In the second part of the current work, we profile the auto-antibody repertoire of DCM patients of the auto-immune subtype. First, we screened a human high density protein array containing 37,500 recombinant proteins deriving from a human fetal brain expression library with plasma. A subset specific for IgG consisting of 48 proteins and a subset specific for the IgG3 subtype containing 32 proteins has been identified. Following high-throughput expression and purification, protein microarrays were generated and incubated with the previously used patient and control plasmas. Following image and data analysis, significant differences between patient and control plasmas have been determined for six proteins on the IgG specific and seven genes on the IgG3 subtype specific protein microarray. We have identified new proteins such as KChIP1, Ma3, cyclin G1, RAD23 and the histone deacetylase 3 as putative specific for DCM, as well as the proteins FADD, BAT3 and tubulin which have been additionally described in other auto-immune diseases. The potassium channel interacting protein 1 (KChIP1) was detected in 9 of 10 patient plasmas. Regarding its function in transient outward current and that defects in the highly homologous KChIP2 protein causes arrhythmias and ventricular tachycardia by absence of the transient outward current, KChIP1 seems to be a very promising candidate.