Parasitic diseases are a major threat to human health and schistosomiasis is second only to malaria for number of people infected. It is spread over 75 tropical and subtropical countries and it is one of the major objectives of the World Health Organization for improving life condition of developing countries. At present only two drugs are used effectively to contrast this nasty parasitic disease, which is chronic and difficult to detect at early stages. Not surprisingly there have been reports of signs of resistance against those drugs. To tackle the problem we have decided to focus our attention on a particular metabolic aspect of the parasite: the uptake of lipids. Shistosomes are not able to de novo synthesise fatty acids, therefore they completely depend on their human host supply. The main proteins known to be involved in intracellular trafficking of lipids are the class of Fatty Acid Binding Proteins (FABPs). Finding significantly different allelic variants is extremely important because of the high homology within the family of eukaryotic FABPs. In the case of Schistosoma mansoni a promising candidate is the truncated isoform of Sm14 (TrSm14) [1], which lacks one entire exon (from aa 81 to aa 116). 3D models of this truncated isoform showed that this exon codes for two whole strands, leading to a $\beta$-barrel with a smaller cavity. The reduced volume of the cavity is connected to a specificity of binding to fatty acids different from the ones capable to bind the full length protein. In particular TrSm14 is capable to bind decanoic acid, which is a short chain FA important in the lipid metabolism of the parasite. Moreover, TrSm14 is sufficiently different from human FABP to be useful both as a vaccine and as a drug target.

Unfortunately, despite the extensive crystallisation conditions tried, using all sort of sparse matrices both commercial and home made, we failed to obtained more than just a few very tiny crystals (40x30x50 $\mu$m). We tested all of them in DESY and proved to be only salt. At present we are strongly considering to end the project, at least under a structural point of view.

References