Despite the efforts to control schistosomiasis, it is still highly prevalent in the world. The treatment is performed with Praziquantel, only drug available. Although it is effective in reducing severe form of the disease, a high reinfection rate remains in endemic areas, added to new infection cases notification. In addition, there are reports of existence of less susceptible parasites to drug. Therefore, new interventions to control and even eliminate the schistosomiasis are needed. The association of vaccination with chemotherapy would be a strategy to control the disease. It is also necessary to develop new diagnostic methods to detect low intensity infections and post treatment cure monitoring. By immunoscreening of adult worm *Schistosoma mansoni* proteome combining two-dimensional electrophoresis and Western blotting (WB-2D) using, for the first time, human serum of infected and naturally resistant individuals from a schistosomiasis endemic area, we have recently identified 47 immunoreactive proteins. But all have cytoplasmic localization. Since the apical membrane of the adult worms and schistosomules tegument is the interface to host's immune system, we started to use protein extraction protocols able to enrich our protein extracts with parasite cell membrane proteins, from the entire worms or only from the tegument. The presence of such proteins in these new extracts was demonstrated by detection of Sm29 by Western blotting and also by shotgun proteomics identification of several *S. mansoni* proteins previously described as tegumental proteins or attached to parasite tegument. After performing 2D-WB experiments with new protein extracts and serum of infected and naturally resistant individuals from schistosomiasis endemic area, we obtained a different spots recognition profile for each serum used, and spots that reacted only to a particular sample serum. The immunoreactive spots of interest, because they are promising targets for the development of schistosomiasis vaccine or diagnostic test, were identified by mass spectrometry.