Studies on Tandem Repeat Antigens from Parasites

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With a large amount of parasite gene sequences available, additional bioinformatic tools to screen these sequences for identifying genes encoding antigens are needed. Proteins containing tandem repeats (TR) are known targets of B cell responses. Genes encoding proteins with TR, consisting of two or more copies of a pattern of nucleotides, have been found in many protozoan parasites, usually by expression cloning methods, although no systematic search for TR-containing proteins has been reported. We became interested in TR proteins when conventional serological screening of a DNA library of *Leishmania infantum*, a causative agent of visceral leishmaniasis, revealed a disproportional number of serological antigens containing TR [1]. The finding made us hypothesize that antigens of serological significance could be identified with a search for TR. In silico screening of the *L. infantum* genome, in fact, succeeded to identify novel antigens with serological significance [2].

Because antibody responses toward TR proteins from parasites have also been found in diseases other than leishmaniasis such as malaria and Chagas' disease, we then explored the validity of this computational screening for other parasitic diseases. Surprisingly, the method showed excellent power in identifying novel antigens from all the examined parasites, i.e., *Trypanosoma cruzi* (a causative agent of Chagas' disease), *T. brucei* (sleeping sickness), *T. congolense* (Nagana), *T. evansi* (Surra), *Schistosoma japonicum* (schistosomiasis) and *S. mansoni* (schistosomiasis). To our knowledge, this is the most powerful computational tool to identify antigens with serological significance from various pathogens.

What is the role of TR proteins in parasite survival? In trypanosomatid parasites, many of the TR proteins are genus- or species-specific, suggesting that the TR genes among the trypanosomatid parasites have evolved along independently. For *Leishmania* parasites it may be beneficial to have such strong B-cell antigens as TR proteins, because B-cells and immunoglobulins help the parasite grow efficiently in their mammalian hosts. In fact, there is up-regulated expression of many *L. infantum* TR proteins in the amastigote stage, the developmental parasite stage that occurs in the mammalian host [3]. These data suggest that how parasites deal with host humoral responses have shaped the repertoire of TR proteins in each species.

Taken together, studies on TR proteins from parasites facilitate antigen discovery for diagnostic and/or vaccine development as well as understanding of host-parasite relationship from immunological and evolutionary points of view.

References

[1] Goto Y., Coler R.N., Guderian J., Mohamath R., Reed S.G.: Infect. Immun., 74: 3939-3945 (2006).
[2] Goto Y., Coler R.N., Reed S.G.: Infect. Immun., 75: 846-851 (2007).
[3] Goto Y., Carter D., Guderian J., Inoue N., Kawazu S.I., Reed S.G.: Infect. Immun., 78: 2138-2145 (2010).