ACQUISITION OF MURINE MAJOR HISTOCOMPATIBILITY COMPLEX GENE PRODUCTS BY SCHISTOSOMULA OF *SCHISTOSOMA MANSONI**

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Schistosomiasis is an excellent example of the evasion of the immune response by a parasite. The trematode worms responsible for this disease can survive for many years inside the blood vessels of vertebrate hosts and are apparently undisturbed by the potent humoral and cell-mediated responses which they have been shown to induce.

Several mechanisms have been postulated to explain the survival of schistosomes in their immunologically hostile environment. Of these hypothetical mechanisms, perhaps the most intriguing is that proposed by Smithers et al. (1). These workers argue that the schistosome may protect itself against immune attack by coating its surface with molecules of host origin. Their hypothesis is based on the observation that worms living in a given host express on their surfaces species specific antigens characteristic of that host. That the acquisition of these determinants may protect the parasite against immune rejection was suggested by further experiments in which it was shown, that as larval schistosomes (schistosomula) acquire host molecules, they lose the capacity to bind antibodies directed against their own surface antigens (2, 3).

The phenomenon of host antigen acquisition by schistosomes has stimulated a number of investigations on the chemical nature of the molecules adsorbed by the worms from the host environment. These studies have suggested that the parasite acquires host material principally in the form of glycolipids. Thus, when cultured together with human erythrocytes of known blood groups, schistosomula acquire A, B, H, and Lewis glycolipid antigens but fail to adsorb other antigens known to exist as glycoproteins (4). Similarly, worms recovered from mice or cultured in the presence of mouse tissue have been shown to express determinants reactive with anti-Forssman antibodies (5).The Forssman antigens have also been characterized as glycolipid molecules.

In the present study, we have used a somewhat different approach to investigate the chemical nature of schistosome acquired host molecules. We have asked whether schistosomula recovered from the lungs of mice belonging to genetically defined inbred strains can be shown to express murine alloantigens. An unexpected finding of this study is that among the host molecules

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adsorbed to the schistosomulum surface are gene products of the murine major histocompatibility complex (MHC).[1]

Materials and Methods

Parasite. Schistosoma mansoni (Puerto Rican strain) is maintained in our laboratory by passage through *B. glabrata* snails and outbred CF_1 mice (Charles River Breeding Laboratories, Wilmington, Mass.). This life cycle was derived from infected and breeder snails originally provided by Dr. Harvey Blankenspoor (University of Michigan, Ann Arbor, Mich.). Schistosomula were prepared from cercariae by an adaptation of the in vitro skin penetration method (6) employing rat instead of mouse skin.

Mice. C3H/HeJ, C57BL/6J, CBA/J, AKR/J, and SJL/J mice were obtained from the Jackson Laboratory (Bar Harbor, Maine). B10/Sn and B10.BR mice were the gift of Dr. Michael Bevan (Massachusetts Institute of Technology). A.TL, A.TH, B6/Ly 1.1, and B6/Ly 1.2 mice were generously provided by Dr. Ulrich Hammerling (Memorial Sloan Kettering Cancer Center, New York). Except where noted, mice of different strains used in the same experiment were matched in terms of their age and sex.

Antisera

B6 ANTI-C3H. C3H anti-B6 alloantisera were prepared by cross-immunization of C3H/HeJ and C57BL/6J mice. Pooled spleen and lymph node cells from donor animals were emulsified in 2 vol of complete Freund's adjuvant and injected into two footpads and two inguinal areas of each mouse (3×10^7 cells/recipient). The animals were then boosted three times at biweekly intervals by intraperitoneal injection with $1.4–3.0 \times 10^7$ spleen and lymph node cells per mouse. 2 wk after the last immunization the animals were bled from the tail vein. The resulting sera (obtained from 20 donors) were combined into a single pool. When tested by indirect immunofluorescence (see below) for its reaction with lymph node cells of the strain used for immunization, each alloantiserum was found to be active at dilutions greater than 1:1,000. Neither serum was found to react with syngeneic indicator cells.

ANTI-(K^k-I^k). This antiserum (D23) is described in the Catalog of Mouse Alloantisera and was obtained from the Transplantation Division, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Md. It was prepared by immunization of (B10 × LP.R III) F_1 mice with B10.A(2R) lymphoid cells and has been found to be specific for K region private specificity 23. The antiserum is also known to be reactive with I^k determinants.

ANTI-K^k. This reagent was prepared by absorbing antiserum D23 with A.TL (K^s-I^k) spleen cells. The absorption was performed by incubating the antiserum with an equal volume of packed spleen cells for 30 min at 4°C. After centrifugation, the supernate was absorbed with a second batch of spleen cells.

ANTI-I^k, I^s. These antisera (A.TL anti-A.TH, A.TH anti-A.TL) were the gift of Dr. Hammerling. When tested in his laboratory, they were found to have cytotoxicity titers of 1:2,500 and 1:1,000, respectively.

ANTI-THY 1. Anti-Thy 1.1 [(C57BL/6J × A/J) anti-B6. PL-Thy 1^a/cy] and anti-Thy 1.2 [(PL/J × B6.PL-Thy 1^a) anti-C57BL/6J] sera were obtained from the Transplantation Division, National Institute of Allergy and Infectious Diseases and are listed in the Catalogue of Mouse Alloantisera.

ANTI-LY 1.1. This antiserum [(BALB/c × E) anti-B6/Ly 1.1] was provided by Dr. Hammerling. The titer of cytotoxic activity of this serum was found to be 1:1,000.

ANTI-H-Y. This antiserum, produced by immunization of female C57BL/6J mice with syngeneic male spleen cells, was generously provided by Dr. Gloria Koo (Memorial Sloan Kettering Cancer Center).

COMMERICALLY PREPARED REAGENTS. Fluorescein conjugates of rabbit anti-mouse Ig; goat anti-rabbit IgG, and rabbit anti-mouse C3 were obtained from N. L. Cappel Laboratories Inc. (Cochranville, Pa.). Unconjugated rabbit antisera to mouse albumin was purchased from the same source.

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[1] *Abbreviations used in this paper*: E/Lac, Earle's lactalbumin medium; FCS, fetal calf serum; FITC, fluorescein conjugated antisera, IMS, serum from *S. mansoni* immune mice; MHC, major histocompatibility complex; NMS, normal mouse serum.

Parasitologic Techniques. Lung stage schistosomula were prepared from mice infected either percutaneously with cercariae (7) or by intravenous injection of schistosomula prepared in vitro (8). Both infection methods were found to produce lung-stage larvae with essentially identical serological properties. 4–6 days after infection the animals were sacrificed and viable schistosomula were recovered from chopped lung fragments according to published procedures (8, 9). To purify the parasites from contaminating lung tissue, the preparations were passed through Nitex nylon screen (100 μm mesh opening) (Tetko, Inc., Elmsford, N.Y.). In several instances, schistosomula were further purified by passage through nylon wool columns followed by two cycles of sedimentation (20 min each) in 15-ml conical centrifuge tubes (BioQuest, BBL, Falcon Products, Becton, Dickinson & Co., Cockeysville, Md.). Similar techniques were employed for the isolation of schistosomula from the ear pinnae of mice after percutaneous infection with cercariae (10). All purification steps were performed in Earle's lactalbumin (Flow Laboratories, Inc., Rockville, Md.) containing 5% fetal calf serum (E/lac-FCS).

Parasite Tissue Culture. Lung schistosomula purified by nylon wool filtration and sedimentation were distributed in aliquots of either 300 or 560 larvae each into 30 ml tissue culture flasks (BioQuest, BBL & Falcon Products) containing E/lac plus 30% FCS or 15% FCS plus 15% mouse serum and antibiotics (penicillin, streptomycin). Where indicated, cultures were also supplemented with 1% (vol/vol) mouse cells (spleen or spleen plus lymph node). The tissue cultures were then maintained for either 19 h or 5 days at 37°C in an incubator gassed with 5% CO_2. At the end of the incubation period, the worms were harvested from the cultures and washed three times by centrifugation (15 s, 550 g).

Immunofluorescence Assays. Schistosomula in aliquots of 20–50 worms each were distributed into 6 × 50-mm glass tubes (Fisher Scientific Co., Pittsburgh, Pa.) in a vol of 0.1 ml. An equal volume of a 1:5 dilution of antiserum or normal mouse serum in E/lac-FCS was then added to each tube and the reaction mixtures incubated for 1 h at 37°C. The larvae were then washed three times by centrifugation (15 s, 250 g) and resuspended to 0.1 ml. An equal volume of a 1:5 dilution of fluorescein-conjugated antiserum (rabbit anti-mouse Ig or goat anti-rabbit Ig) was next added to the parasites. After incubation for 30 min at 23°C, the larvae were washed three times by centrifugation and resuspended in 50 μl of phosphate-buffered 40% glycerol (pH 7.4). A similar protocol was followed in testing the reactivity of antisera with cell populations. Approximately 10^5-10^6 pooled lymph node cells were tested per assay. Incubation of the cells with fluorescein conjugate was performed at 4°C.

Test samples were transferred to slides which were then mounted with coverslips and examined at either 250 × (worms) or 1,000 × (cells) with a Leitz fluorescence microscope. 10 larvae were examined per sample. A worm was scored as positive when there was defined staining of the tegumental surface. In addition, reactions were scored as either weakly (+) or strongly (++) positive. Cell reactions were assessed by examining 100 cells and scoring the number with positive membrane fluorescence.

Results

Schistosomula Acquire MHC as Well as Non-MHC Coded Alloantigens. The presence of alloantigens on lung stage schistosomula was established in the experiment summarized in Table I. Larvae obtained from C3H mice were shown to react with an alloantiserum of broad specificity produced by immunization of C57BL/6 mice with C3H lymphoid cells. The same worms failed to react with an antiserum produced in C3H mice against C57BL/6 cells. Conversely, larvae obtained from C57BL/6 mice were found to react with the anti-C57BL/6 alloantiserum but not with the alloantiserum produced against C3H determinants.

To determine whether or not MHC coded products were among the alloantigens acquired by lung stage schistosomula, we assayed worms recovered from congenic mice for their reactivity with the same alloantisera (Table I). As expected, larvae recovered from C57B10/Sn mice, which possess the H-2ᵇ haplotype, reacted with the anti-C57BL/6 but not with the anti-C3H alloantise-

TABLE I
Acquisition of Murine Alloantigens by Lung Stage
Schistosomula

Strain of worm donors	H-2 Haplotype	Positively staining worms with the following sera	
		C57 Anti-C3H	C3H Anti-C57
C3H/He	k	10/10*	0/10
C57BL/6	b	0/10	10/10
B10/Sn	b	0/10	10/10
B10.BR	k	10/10	10/10

* Number of schistosomula with positive tegumental fluorescence per total worms scored.

rum. In contrast, worms obtained from B10.BR mice, derived by breeding the H-2^k genotype into the C57BL/10 background, did react with the anti-C3H serum suggesting that they had acquired H-2^k determinants recognizable by the anti-C3H (H-2^k) alloantiserum. However, since the B10.BR (H-2^k) worms also reacted with the anti-C57BL/6 (H-2^b) alloantiserum, it was clear that other alloantigens in addition to those coded for by the MHC were being acquired by the parasites.

Both K and I Coded Antigens Are Expressed on the Schistosomulum Surface. To determine which MHC products are acquired by lung stage schistosomula, we tested the reactivity of worms from different inbred and inbred recombinant strains for their reactivity with antisera directed against antigens coded for by distinct regions of the major histocompatibility locus (Table II). The first antiserum tested, anti-(K^k + I^k), was directed against k allelic products of both the K and I regions of the locus. Since this antiserum was produced by immunization against cells of B10.A (2R) mice which possess the haplotype (K^k, IA^k, IB^k, IC^d, S^d, D^b), the only k antigens which the reagent is capable of detecting are those coded for by K, IA, and IB genes. When tested with worms recovered from CBA, A.TL, A.TH, or SJL mice, the antiserum was found to react with CBA and A.TL worms but not with worms obtained from A.TH or SJL donors. This finding indicated that lung stage schistosomula acquire I and possibly K coded antigens. As example of a positive reaction between a schistosomulum recovered from CBA lungs and the antiserum is shown in Fig. 1. The acquisition of Ia determinants by schistosomula was confirmed by demonstrating reactions between Ia-specific antisera and worms obtained from the appropriate genetic background (Table II). Thus, the anti-I^k alloantiserum reacted with CBA and A.TL worms but not with A.TH or SJL worms. Conversely, the anti-I^s alloantiserum reacted with SJL and A.TH worms but not with CBA or A.TL larvae.

The surface acquisition of K coded antigens was established by demonstrating reactions between an anti-K^k alloantiserum and worms recovered from CBA mice. As expected, the antiserum failed to react with worms obtained from the lungs of A.TL, A.TH, or SJL mice.

Murine Alloantigens and Serum Proteins Not Detected on Schistosomula. To determine whether or not the surface acquisition of MHC products by schisto-
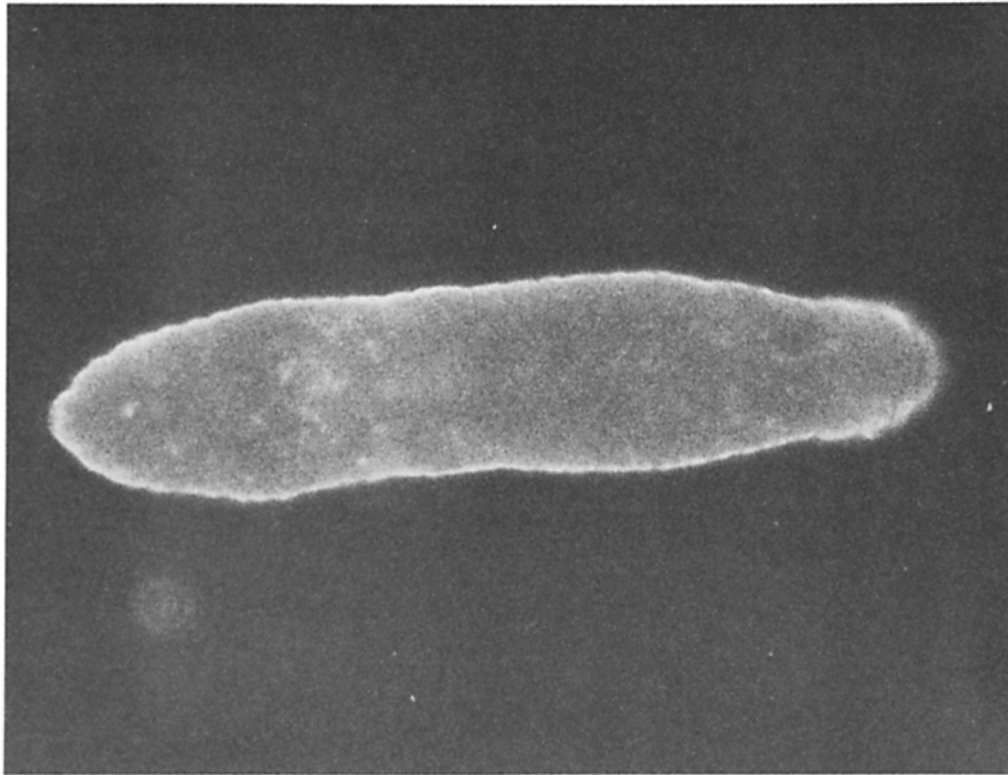
Fig. 1. Photomicrograph showing the reaction of anti-H-2^k (K^k + I^k) antibody with a schistosomulum recovered from CBA (H-2^k) mice ($\times$ 750).

TABLE II

Acquisition of K and I Coded Determinants by Lung Stage Schistosomula

Strain of worm donors	Positively staining larvae with the following sera			
	Anti-(K^k + I^k)*	Anti-K^k	Anti-I^k	Anti-I^s
CBA (K^k-I^k)	10/10	10/10	10/10	0/10
A.TL (K^s-I^k)	7/10	0/10	9/10	0/10
A.TH (K^s-I^s)	0/10	0/10	0/10	10/10
SJL (K^s-I^s)	0/10	0/10	0/10	10/10

* The antisera used in this experiment are described in detail in Materials and Methods.

somula is selective, larvae were examined for the presence of other known alloantigens and serum proteins. The cell surface alloantigens assayed for were Thy 1, Ly 1, and H-Y. As summarized in Table III, none of these antigens could be detected on lung stage schistosomula although the individual alloantisera did give positive reactions with lymphoid cells from the appropriate worm donors.

Lung stage larvae were also examined for the presence of bound serum

TABLE III

Murine Alloantigens Not Detected on Schistosomula

Strain of worm of LN cell donors	Relevant phenotype	Positively staining worms or LN cells with the following sera					
			NMS*	Anti-Thy 1.1	Anti-Thy 1.2	Anti-Ly 1.1	Anti-H-Y
B6/Ly 1.1	Ly 1.1	Worms	0/10	—	—	0/10	—
		Cells	9/100‡			57/100	
B6/Ly 1.2	Ly 1.2	Worms	0/10	—	—	0/10	—
		Cells	6/100			5/100	
AKR/J	Thy 1.1	Worms	0/10	0/10	0/10	—	—
		Cells	7/100	83/100	9/100		
C57BL/6	Thy 1.2	Worms	0/10	0/10	0/10	—	0/10
(Female)	H-Y⁻	Cells	8/100	14/100	78/100		32/100
C57BL/6	H-Y⁺	Worms	0/10	—	—	—	0/10
(Male)		Cells	18/100				75/100

* NMS, normal C57BL/6 serum.
‡ Number of cells with positive membrane fluorescence.

TABLE IV

Murine Serum Proteins Not Detected on Lung Schistosomula

Worms tested	Positively staining larvae with the following reagents		
	Rabbit anti-albumin FITC* Anti-rabbit IgG	FITC Anti-mouse Ig	FITC Anti-mouse C3
Lung schistosomula	0/10	0/10	0/10
3-h old schistosomula:			
Pretreated with fresh NMS	—	—	10/10
Pretreated with IMS	—	10/10	—

* FITC, fluorescein-conjugated antiserum; NMS, normal mouse serum; IMS, immune serum from C57BL/6 mice infected for 12 wk with 30 cercariae each.

proteins. Neither immunoglobulin (Ig) nor the third component of complement (C3) could be detected by direct immunofluorescence on the surface of lung stage parasites (Table IV). In control experiments, the same fluorescein conjugated reagents (anti-Ig or anti-C3) were shown to give positive reactions when tested against early (newly transformed) schistosomula pretreated either with immune mouse serum containing antibodies directed against schistosome surface antigens or with fresh mouse serum as a source of complement. The detection of bound Ig or C3 on early schistosomula has been described previously (11). Similarly, when tested by indirect immunofluorescence, mouse albumin could not be detected on the surface of lung stage schistosomula.

Acquisition of MHC Coded Antigens by Skin Stage Schistosomula. Schistosomula recovered from the skin of percutaneously challenged animals were also shown to possess surface host MHC products. When recovered either 22 or 45 h after infection from the ear pinnae of CBA mice, these skin schistosomula stained positively with the antiserum directed against K^k and I^k determinants

TABLE V

Acquisition of MHC Coded Antigens by Schistosomula Recovered
from Skin after Cercarial Infection

After percu-taneous chal-lenge	Worm donor	Positively staining larvae with the following sera	
		NMS	Anti-$(K^k + I^k)$*
h			
22	CBA(H-2^k)	0/10	5/5
	C57BL/6(H-2^b)	0/9	1/10
45	CBA(H-2^k)	0/10	10/10
	C57BL/6(H-2^b)	0/7	0/10

* Mouse sera were used in this experiment at a final dilution of 1/40.
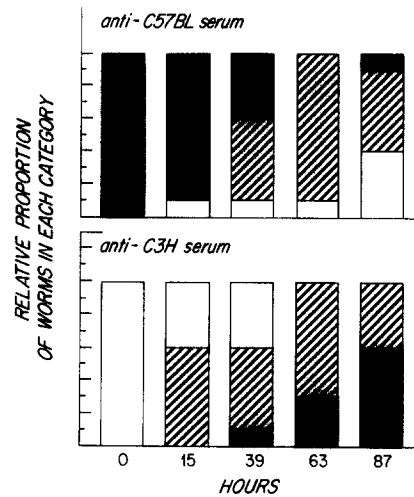

FIG. 2. Exchange of alloantigens after intravenous transfer of lung schistosomula re-covered from C57BL/6 mice into C3H/He recipients. At times indicated groups of C3H/He mice were sacrificed and the transferred schistosomula recovered from the lungs. The schistosomula were then mixed with either C3H anti C57BL/6 serum (top panel) or C57BL/6 anti-C3H serum (bottom panel) or normal mouse serum (not shown), washed and treated with fluorescein-conjugated rabbit anti-mouse IgG. The schistosomula were then examined by fluorescence microscopy and scored either as negative (white), weakly positive (cross-hatched), or strongly positive (black). In each assay 10 worms were scored. Worms tested with normal mouse serum were negative at each of the time points.

(Table V). Worms recovered at the same time periods from C57BL/6 mice were, except for one organism, negative when tested with the same antiserum.

In Vivo and in Vitro Uptake and Exchange of Alloantigens on the Larval Surface. To study the stability of the association between alloantigen and the parasite surface, worms recovered from the lungs of C57BL/6 animals were reinjected intravenously into the lungs of C3H mice. At various times after-wards, the larvae were recovered and tested for the presence of either C57BL/6 or C3H alloantigens. As expected, 10/10 of the donor worms stained positively with the anti-C57BL/6J antisera before reinjection and all failed to react with the anti-C3H antiserum (Fig. 2). However, when recovered as early as 15 h

TABLE VI

In Vitro Acquisition of MHC Antigens by Lung Stage Schistosomula from C57BL/6 Donors

Exp.	Duration of culture	Cells or sera added to culture	Positively staining worms with the following sera		
			NMS	Anti-C3H	Anti-$(K^k + I^k)$
1	5 days	C3H Spleen cells	0/5	10/10	4/10
		C3H Serum	NT*	0/10	0/10
		C57BL/6 Spleen cells	NT	0/10	0/10
2	19 h	CBA Spleen + LN cells	0/10	NT	10/10
		C57BL/6 Spleen + LN cells	0/10	NT	1/10

* NT, not tested

after reinjection into allogeneic recipients, C3H determinants could be detected on a proportion of the larvae. The number of positive worms was found to increase with time such that by 87 h, 100% of the larvae expressed surface C3H antigens. At the same time, the worms were observed progressively to lose their C57BL/6 antigens. However, worms staining positively with the anti-C57BL/6 reagent could still be observed at the termination of the experiment, 87 h after reinjection.

Schistosomula could also be demonstrated to acquire alloantigens when cocultivated with lymphoid cells in vitro. As summarized in Table VI, C3H alloantigens as well as H-2^k determinants could be detected on worms from C57 donors as early as 19 h after culture with C3H spleen and lymph node cells. Although alloantigen uptake could be demonstrated on worms cocultured with cells, no uptake was evident when allogeneic serum was used as the source of host antigen.

Discussion

The data presented here indicate that *S. mansoni* schistosomula recovered from mice or cultured in the presence of murine lymphoid cells express alloantigens among which are gene products of the MHC. These molecules are almost certainly acquired from host tissue rather than synthesized by the parasites. Indeed, the elaboration of these alloantigens by the larvae would require that they possess not only a recognitory system for distinguishing between different alloantigens in their environment, but also the capacity to respond by producing a molecule of the appropriate structure. Moreover, since dead schistosomula incubated in the presence of host tissue can be shown to express antigens of that tissue (12), it is reasonable to assume that the schistosome-bound alloantigens characterized in the present study are also of host rather than parasite origin.

Previous studies have suggested that the host molecules acquired by schistosomes are glycolipid in nature. Goldring and colleagues demonstrated that schistosomula cultured in the presence of human blood of known serological type acquire A, B, H, and Lewis blood group antigens (4). Since the larvae were found to express A antigens after culture in serum from individuals of A blood group type who were either secretors or nonsecretors, these authors hypothe-

sized that the A, B, and H blood group antigens are acquired by the worms in glycolipid form. The finding that other blood group antigens (e.g., M, N, rhesus, and Duffy) known to exist as glycoproteins were not detectable on cultured schistosomula supported this hypothesis. Finally, by cocultivating schistosomula with erythrocytes surface labeled with ^{3}H, Goldring and colleagues were able to demonstrate the transfer of a low molecular weight glycolipid-like substance from the cells to the worms (13). In another series of experiments, Dean and Sell (5) demonstrated the presence of a Forssman-like antigen on adult worms recovered from mice or on schistosomula after incubation in mouse tissue. Since the Forssman antigens are also thought to exist as glycolipids, their findings also support the hypothesis that host molecules are acquired by schistosomes principally in the form of glycolipids.

This concept must now be modified in the light of the evidence reported in the present study. As indicated by our data, two classes of nonglycolipid molecules, the K and I gene products, can be acquired by schistosomula as host antigens. Previous work has indicated that the K region product is a glycoprotein of 47,000 mol wt (14), whereas Ia antigens apparently exist either as a cell-associated glycoprotein consisting of two polypeptide chains of about 25,000 and 35,000 mol wt (15) or as soluble low molecular weight carbohydrates (16). Thus, it is clear that host molecules other than glycolipids may associate themselves with the schistosome surface. The biochemical form in which these glycoprotein and/or carbohydrate host substances bind to the parasite's tegument remains to be determined.

The acquisition of K and Ia host molecules by schistosomes appears to be at least partially selective. Thus, we were unable to detect on K and Ia bearing schistosomula the murine cell surface antigens, Thy 1, Ly 1, and H-Y or the mouse serum proteins, albumin Ig or C3 (Tables III and IV). Nevertheless, it is clear, both from the previous demonstration of Forssman antigen on mouse schistosomes and from the reactivity of larvae from B10.BR mice with the C3H anti-C57BL/6 alloantiserum (Table I), that host molecules other than K and I region products are acquired by schistosomes during murine infection. Whether MHC products constitute a major or minor portion of the total population of host molecules associated with the parasite's surface is a question which we are now attempting to answer by means of quantitative immunochemistry.

The finding of MHC products associated with the surface of a mammalian parasite poses somewhat of a paradox. Over the past several years, considerable evidence has been obtained indicating that MHC determined molecules play a central role in immune recognition and cell co-operation (17). Thus, by analogy with previous work on virus infected (18) and chemically modified (19) cell targets, one might expect the presence of K region products on lung schistosomula to facilitate their recognition and rejection by the immune system. Nevertheless, it appears that schistosomula, by the time they reach the lung stage, are completely refractory to immune attack by both T cell and antibody-mediated effort mechanisms (8, 10, 20). Thus, in the case of schistosomula, at least, the association of MHC product with target does not seem to promote its killing.

On the contrary, it is possible that K and I region coded molecules, as acquired host antigens, protect the surface of the parasite from immune at-

tack rather than promote its recognition. Several lines of evidence point to a role for host molecules in disguising the schistosome tegument and thereby preventing its recognition by immune effector mechanisms. As already noted, an inverse correlation has been observed in the presence of host molecules on schistosomula and their ability to bind antibodies directed against parasite antigens (2, 3). Thus, newly-transformed schistosomula lack host antigens and are highly reactive with anti-parasite antibodies while lung stage schistosomula possess a dense coat of host molecules and are unable to bind antibodies directed against the same parasite antigens. Further evidence for a protective role of acquired host molecules has recently been obtained in a series of experiments in which the effects of cultivation in vitro on the survival of schistosomula subsequently transferred into immune mice has been studied. In this work, it was shown that culture in mouse erythrocytes as a host molecule source had a significant effect in promoting the survival of schistosomula when they were then injected intravenously into immune mice (20).

Although the above evidence suggests that the acquisition of host molecules protects the schistosome surface from immune attack, it has been argued that other changes in the developing parasites may be responsible for their evasion of the immune response. Thus, Dean has observed that schistosomula maintained in a tissue culture medium devoid of host molecules become refractory to in vitro attack by antibody and complement (21). In addition, complex changes in the architecture of the parasite's tegument are known to occur during the same time period that schistosomula acquire host molecules in vivo (22). The above changes include the development of a double unit membrane and the redistribution of intramembranous particles in that membrane. Structural modifications of this type could account for the insusceptibility of older schistosomula to damage by antibody-dependent as well as T-cell-mediated killing mechanisms.

Thus, at present, the biological significance of the association of MHC products with schistosomula is unclear. As molecules which appear to play a fundamental role in the discrimination of self from nonself, MHC coded products would appear to be ideally suited as a biochemical disguise for parasites of vertebrate hosts. However, to test the latter hypothesis, it will be necessary to demonstrate formally that schistosomula coated artificially with purified MHC coded molecules are more resistant to immune attack then untreated larvae. This is the experimental approach currently being followed in our laboratory.

Summary

Schistosoma mansoni schistosomula recovered from the lungs of inbred mice were shown to possess serologically detectable alloantigens on their tegumental surfaces. Using appropriate antisera and infected congenic and recombinant mice as worm donors, gene products of the K and I subregions of the major histocompatibility complex were demonstrated among these alloantigens acquired by the parasites. In contrast, other cell surface alloantigens, such as Thy 1, Ly 1, and H-Y and the serum proteins albumin, C3 and Ig, could not be detected on the surface of lung schistosomula by means of comparable techniques. In another series of experiments, schistosomula recovered from the lungs of mice and reinjected into allogeneic recipients were shown to exchange their alloantigens during an 87-h period of examination. Similarly, lung

schistosomula cocultured with allogeneic lymphocytes were shown to acquire major histocompatibility complex (MHC) coded antigens from the cells. It is possible that as acquired host molecules, MHC gene products may disguise the surface of schistosome parasites thereby rendering them insusceptible to immune attack.

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