Characterization of *Entamoeba histolytica* Intermediate Subunit Lectin-Specific Human Monoclonal Antibodies Generated in Transgenic Mice Expressing Human Immunoglobulin Loci

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Four fully human monoclonal antibodies (MAbs) to *Entamoeba histolytica* intermediate subunit lectin (Igl) were prepared in XenoMouse mice, which are transgenic mice expressing human immunoglobulin loci. Examination of the reactivities of these MAbs to recombinant Igl1 and Igl2 of *E. histolytica* showed that XEhI-20 [immunoglobulin G2(α)] and XEhI-28 [IgG2(α)] were specific to Igl1, XEhI-B5 [IgG2(α)] was specific to Igl2, and XEhI-H2 [IgM(α)] was reactive with both Igl1 and Igl2. Gene analyses revealed that the V\(_{H}\) and V\(_{\text{germ}}\) germ lines were VH3-48 and L2 for XEhI-20, VH3-21 and L2 for XEhI-28, VH3-33 and B3 for XEhI-B5, and VH4-4 and A19 for XEhI-H2, respectively. Flow cytometry analyses showed that the epitopes recognized by all of these MAbs were located on the surface and in the cytoplasm, but different localization patterns in intracellular vacuoles were also present. The preincubation of trophozoites with XEhI-20, XEhI-B5, and XEhI-H2 caused significant inhibition of the adherence of trophozoites to Chinese hamster ovary cells, whereas preincubation with XEhI-28 did not do so. XEhI-20, XEhI-B5, and XEhI-H2 were injected intraperitoneally into hamsters 24 h prior to intrahepatic challenge with *E. histolytica* trophozoites. One week later, the mean abscess size in groups injected with one of the three MAbs was significantly smaller than that in controls injected with polyclonal IgG or IgM isolated from healthy humans. These results demonstrate that human MAbs to Igls may be applicable for immunoprophylaxis of amebiasis.

Amebiasis caused by infection with *Entamoeba histolytica* is one of the most problematic parasitic diseases of humans worldwide. It is estimated to result in 50 million cases of colitis and liver abscess and up to 100,000 deaths annually (54). However, an effective vaccine or chemoprophylaxis to prevent amebiasis has not been developed. The adherence of *E. histolytica* trophozoites to colonic mucins and various host cells is an essential event for colonization, invasion, and subsequent pathogenesis. The adherence is mediated by a galactose (Gal)- and N-acetyl-D-galactosamine (GalNAc)-inhibitable lectin (39). The lectin is a 260-kDa heterodimeric glycoprotein composed of a 170-kDa heavy subunit (Hgl) and a 31- or 35-kDa light subunit (Lgl) (38), and the Hgl is a candidate vaccine for amebiasis (22, 27, 30). We have demonstrated previously that a 150-kDa intermediate subunit (Igl), which is noncovalently associated with Hgl, also contributes to adherence (13). A mouse monoclonal antibody (MAb) specific for Igl significantly inhibits the adherence and cytotoxicity of trophozoites to mammalian cells and inhibits erythropagocytosis (10, 48, 51). The immunization of hamsters with native Igl can inhibit liver abscess formation (11). There are two isoforms of Igl, which have 1,101 and 1,105 amino acids and are referred to as Igl1 and Igl2, respectively (9). The Igls are known to be cysteine-rich proteins containing multiple CXXC motifs, but the association between inhibitory effects and each Igl isoform is not well understood.

Recent studies have shown that cellular immunity is important for the prevention of invasive amebiasis (26, 42). However, it has been reported previously that passive immunization with rabbit antiserum to a serine-rich *E. histolytica* protein, with human anti-*E. histolytica* antibodies obtained from patients with amebic liver abscesses, or with a mouse MAb to a surface lipophosphoglycan antigen inhibits amebic liver abscess formation in a severe combined immunodeficient mouse model (31, 43, 55). We have also demonstrated previously that mouse MAb to Igl can inhibit liver abscess formation in hamsters (12). Therefore, human MAbs to these antigens may be applicable to reduce mortality from amebiasis by passive immunization. Hybridoma technology has been relatively unsuccessful for the generation of human MAbs, but several new methods have recently been developed (3, 5, 53), including the use of XenoMouse mice, which are transgenic mice containing the megabase-sized human immunoglobulin loci (17, 18, 32). Several human MAbs generated using this approach are now in clinical trials (4, 14, 28, 37).

In the present study, we used XenoMouse mice to generate fully human MAbs to *E. histolytica* Igl. Here, we report the molecular characterization of human MAbs specific for Igl1 and Igl2 of *E. histolytica*, and we also evaluate the effects of these human MAbs on amebic adherence in vitro and amebic liver abscess formation in hamsters.

**MATERIALS AND METHODS**

**Cultivation of parasites.** Trophozoites of the *E. histolytica* HM-1:IMSS strain were axenically cultured in TY1-S-33 medium supplemented with 15% adult...
bovine serum at 37°C (15). Cultured trophozoites were harvested in the loga-
thetic phase of growth and used in subsequent experiments.

Production of MAbs. XenoMouse 2a3 strain male mice, which express human immunoglobulin M (IgM), IgG2, and immunoglobulin κ genes, were provided by Abgenix, Inc. (Fremont, CA). Native Ig was purified from trophozoites of *E. histolytica* HM-1:IMSS by immunofinity column chromatography using mouse MAb E3H015 (13). XenoMouse mice were immunized intraperitoneally with 10 μg of Ig emulsified in complete Freund's adjuvant. The mice then received two booster inoculations of Ig in incomplete Freund's adjuvant at 2-week intervals. After an additional 4 weeks, the mice received Ig only. On day 4 thereafter, spleen cells were isolated and fused with X63-Ag8.653 mouse myeloma cells in 50% polyethylene glycol 1500. Hybridomas secreting MAbs against *E. histolytica* trophozoites were screened by immunofluorescent staining and cloned by limi-
iting dilution. Immunoglobulin isotypes of MAbs were determined by immuno-
fluorescent staining using subtype-specific secondary antibodies. Hybridomas were

Cloning and sequencing of immunoglobulin genes. Total RNA was purified from hybridomas and subjected to reverse transcription-PCR as described pre-
viously (47). Genes coding for the light (κ) chain and the Fd regions of the heavy (γ and μ) chains were amplified by 30 cycles of PCR. The light-chain genes were first ligated with an expression vector, pFab-His2, and introduced into Esche-
richia coli JM109 cells. The vector with insert was then ligated with the E. coli heavy-chain genes introduced into the expression vector. The production of

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Immunofluorescent staining for screening. Indirect immunofluorescent stain-
ing of fixed *E. histolytica* trophozoites was performed as described previously (50), except that 4% paraformaldehyde was used as the fixative. Fluorescin isothio-
cyhanate (FITC)-conjugated goat antibodies to human IgG (H and L), human IgFab, human IgG2, and human IgM (ICN Pharmaceuticals) were used as secondary antibodies.

Confocal microscopy. Trophozoites of the *E. histolytica* HM-1:IMSS strain were fixed with 4% paraformaldehyde in phosphate-buffered saline (PBS) for 30 min and attached to silane-coated glass slides by using a Cytoxpin 2 centrifuge (Shandon, Oakland, CA). After being washed with PBS, the glass slides were incubated with 10% sucrose in PBS for 1 h and then stored at −80°C until use. The trophozoites were treated with 0.05% Triton X-100 in PBS for 5 min. After being washed with PBS, the trophozoites were blocked with 3% bovine serum albumin in PBS for 30 min and then incubated for 1 h at room temperature with labeled MAbs. An Alexa Fluor 488 protein labeling kit and an Alexa Fluor 594 protein labeling kit (Molecular Probes, Eugene, OR) were used for the labeling of MAbs. After being blocked, the stained trophozoites were washed with PBS and attached to silane-coated glass slides by using a Cytospin 2 centrifuge. The adherence of trophozoites of the *E. histolytica* was determined by examining 300 trophozoites. Statistical analysis was performed by Student's t test.

Passive immunization and hepatic challenge. Male Syrian hamsters weighing 95 to 110 g were purchased from Japan SLC, Inc. (Hamamatsu, Japan). Each hamster received an intraperitoneal injection of 0.5 ml of PBS containing 5 mg of *E. histolytica* Igl2 proteins as described previously (47). For the preparation of an *E. histolytica* Ig2 fragment encompassing the full-length protein except for the signal sequences, a DNA fragment was obtained by PCR amplification of genomic DNA (HM-1:IMSS strain) with primers 5'-CTG ATG TAA ATG AAA AAT GTA-3' and 5'-CCC TCG TGG GTA TAA GAT TCT TGA CCA TT-3'. Three DNA fragments encoding the N-terminal region (aa 14 to 382), the middle region (aa 294 to 757), and the C-terminal region (aa 604 to 1092) of *E. histolytica* Ig2 were also obtained by PCR amplification of DNA encoding full-length Ig2. The primers

RESULTS

Specificity of human MAbs. Four human MAbs designated XEhI-20, XEhI-28, XEhI-B5, and XEhI-H2 were used in the study. Indirect immunofluorescent antibody staining using subtype-specific secondary antibodies showed that three of the MAbs, XEhI-20, XEhI-28, and XEhI-B5, were IgG2, while XEhI-H2 was IgM. The reactivities of the human MAbs to recombinant Ig1 and Ig2 from *E. histolytica* were examined by dot blot analysis. XEhI-20 and XEhI-28 were specifically re-
active with Ig1, whereas XEhI-B5 was specific to Ig2. The
remaining MAb, XEH-H2, was reactive with both Igls, as well as with sera from immune XenoMouse mice, indicating the presence of a common epitope in these proteins. The reactivities of the MAbs to native proteins were also examined by Western immunoblot analysis (Fig. 1). Under nonreducing conditions, immune sera and XEH-H2 recognized two bands with apparent molecular masses of 150 and 170 kDa. XEH-20 and XEH-28 were reactive with the 170-kDa band, and XEH-B5 was reactive with the 150-kDa band, indicating that the upper band was Ig1 and the lower band was Ig2.

Primary structures and gene usage patterns of human MAbs. Immunoglobulin genes from hybridomas secreting human MAbs were cloned and sequenced. As shown in Fig. 2, the primary structures of both the heavy and light chains of the four MAbs were different. However, similarity between the complementarity-determining regions in the light chains of XEH-20 and XEH-28 was found, while the complementarity-determining regions in the heavy chains of these two MAbs were quite different. Sequence analysis of the constant regions of the heavy chains also showed that XEH-H2 was IgM. The sequence homology of these MAbs to germlines was analyzed using the IgBLAST program. Three V segments of the heavy chains belonged to the family VH3, but their germ lines were different, and the remaining one (in XEH-H2) was a member of the VH4 family (Table 1). The D segments differed among these MAbs, but the J segments were of the JH4 family in all except XEH-20. The germ lines of both the V and J segments of the light chains in XEH-H2 and XEH-28 were identical.

Affinity of human MAbs. The affinity of human MAbs to Ig1 was evaluated by surface plasmon resonance. The dissociation constants of the four MAbs ranged from $1.24 \times 10^{-8}$ to $1.77 \times 10^{-10}$ M (Table 2). The affinity of XEH-28 was clearly lower than those of the other MAbs.

Epitopes recognized by human MAbs. Living trophozoites were incubated with MAbs, fixed, and then subjected to flow cytometry analysis. As shown in Fig. 3, all of the MAbs were reactive with the cells, suggesting that the epitopes exist on the cell surface. The reactivities of MAbs to partial fragments of *E. histolytica* Ig1 were also examined by dot blot analysis. XEH-28 was reactive with the Ig1 N-terminal fragment (aa 14 to 382), but not with the middle region (aa 294 to 753) or the Ig1 C-terminal fragment (aa 603 to 1088). In contrast, XEH-H2 was reactive with the Ig1 middle and C-terminal fragments, suggesting the localization of the epitope between aa 603 and 753. Since XEH-20 and XEH-B5 did not react with any partial fragments, these MAbs seem to recognize a particular conformation of Ig1. To further evaluate the effect of the protein conformation on the binding of MAbs, recombinant

<table>
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<td>S.Y.M.Y.M.P.</td>
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<td>RIVMTQSSAPLMSGQGERATLSC</td>
<td>RASQSISS.-------NF-A</td>
<td>WYQQKPGSSPRLLY</td>
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FIG. 1. Western immunoblot analysis of human MAbs to *E. histolytica*. Lysates of trophozoites from the HM-1:IMSS strain were subjected to SDS-PAGE in a 7.5% gel under nonreducing conditions and transferred onto polyvinylidene difluoride membranes. The strips were treated with the following: lane 1, sera from preimmune XenoMouse mice; lane 2, sera from XenoMouse mice immunized with native *E. histolytica* Ig1; lane 3, XEH-28; lane 4, XEH-20; lane 5, XEH-B5; and lane 6, XEH-H2. HRP-conjugated goat antibody to human IgG(H+L) was used as a secondary antibody. The numbers on the right indicate molecular masses of size markers.

FIG. 2. Deduced amino acid sequences corresponding to genes coding for heavy- and light-chain variable regions in human MAbs to *E. histolytica* Igls. FR, framework regions; CDR, complementarity-determining regions. Dashes and dots indicate deletions and identical residues, respectively.
Igls were heat treated under nonreducing and reducing conditions and then their reactivities to MAbs were compared with those of native recombinant Igls (Fig. 4). Reactivities to all MAbs were reduced by heat treatment, indicating that the conformation is important for all the epitopes recognized by these MAbs. Reactivity with XEhI-20 decreased clearly under reducing conditions, suggesting that an S-S bond is involved in the epitope. In contrast, the reactivity of XEhI-H2 with Ig1 was relatively retained after heat treatment under reducing conditions.

**Localization of Ig11 and Ig12.** *E. histolytica* trophozoites were double stained with XEhI-20 and XEhI-B5 and then observed by confocal microscopy (Fig. 5). Both Ig11 and Ig12 were detected on the plasma membrane and in the cytoplasm in all trophozoites. Ig11 and Ig12 were colocalized in most cells, but different localization patterns on vacuoles in the cytoplasm were also seen (Fig. 5D).

**Inhibitory effects of human MAbs on amebic adherence.** To examine the effect of human MAbs on amebic adherence, trophozoites were pretreated with 10 μg of human MAbs and then incubated with CHO cells. XEhI-20, XEhI-B5, and XEhI-H2 significantly inhibited amebic adherence compared with that of controls treated with PBS only (P < 0.0001 for each MAb), whereas XEhI-28 failed to produce inhibition (Fig. 6). The inhibitory effect of XEhI-B5 was significantly greater than those of XEhI-20 and XEhI-H2 (P = 0.0029 and 0.0284, respectively). The effect of XEhI-H2 was also significantly greater than that of XEhI-20 (P = 0.0212).

**Effects of human MAbs on liver abscess formation.** The three human MAbs showing neutralizing activity toward amebic adherence in vitro were further examined for their effects on amebic liver abscess formation in an animal model (Fig. 7). All of 12 hamsters treated with PBS only developed liver abscesses following infection with *E. histolytica*, with a mean percentage of abscessed liver of 42.7%. In two other control groups receiving 5 mg of IgG or IgM, the mean percentages of abscessed liver were 39.7 and 45.4%, respectively. When hamsters were passively immunized with 5 mg of XEhI-20, XEhI-B5, or XEhI-H2 24 h before infection, the mean percentage of abscessed liver was 13.9, 14.7, or 20.9%, respectively, and these values were significantly lower than those for animals immunized with isotype controls (XEhI-20 versus IgG control, P < 0.0001; XEhI-B5 versus IgG control, P < 0.0001; XEhI-H2 versus IgG control, P < 0.0001).

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<th>(K_d) (M)</th>
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<td>XEhI-28</td>
<td>Ig11</td>
<td>8.03 × 10(^{10})</td>
<td>1.24 × 10(^{-8})</td>
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<tr>
<td>XEhI-B5</td>
<td>Ig12</td>
<td>5.65 × 10(^{9})</td>
<td>1.77 × 10(^{-10})</td>
</tr>
<tr>
<td>XEhI-H2</td>
<td>Ig2</td>
<td>2.26 × 10(^{9})</td>
<td>4.43 × 10(^{-10})</td>
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**FIG. 3.** Flow cytometric analysis of *E. histolytica* trophozoites stained with human MAbs to Igls (black-filled histograms). Intact trophozoites were incubated with human MAbs XEhI-20, XEhI-28, XEhI-B5, and XEhI-H2, followed by FITC-conjugated goat antibody to human IgG(H+L). The control was stained only with a secondary antibody (unfilled histograms). A representative histogram for each antibody is depicted. Fluorescence levels are expressed in arbitrary units.
versus IgM control, $P = 0.0003$). In the group treated with XEhI-20, no abscesses were found in three hamsters.

**DISCUSSION**

In the present study, human MAbs specific for Ig1 and Ig2 were successfully generated in XenoMouse mice. This is the first report concerning the production of fully human MAbs against *E. histolytica*. Native Ig1 purified using mouse MAb EH3015 was used for immunization, and the results indicated that the native Ig1 fraction contained both Ig1 and Ig2. In our previous study, SDS-PAGE analysis of the native Ig1 gave two bands with molecular masses of 150 and 170 kDa (11, 13). Western immunoblot analysis has also shown that MAb EH3015 recognizes 150- and 170-kDa molecules in the H-302: NIH strain of *E. histolytica* (48). The present study revealed that the 170-kDa band is Ig1 and the 150-kDa band is Ig2, although the molecular mass calculated from the DNA sequence is larger for Ig2 than for Ig1 (9).

Neutralizing activity toward amebic adherence to CHO cells was detected for both Ig1- and Ig2-specific human MAbs. Therefore, both Igls must be involved in amebic adherence. Since XEhI-28 did not affect amebic adherence to CHO cells, the N terminus of Ig1 may not be important for adherence to host cells. When the conformation of the recombinant Igls was changed by heat treatment, reductions in the reactivities of all MAbs were observed. Therefore, the epitopes recognized by these MAbs seem to be discontinuous. Indeed, XEhI-20 and XEhI-B5 reacted with full-length Ig1 molecules but failed to react with three partial fragments. Since the reactivity of XEhI-H2 was relatively retained after heat treatment under reducing conditions, we cannot exclude the possibility that its epitope is continuous. The presence of many cysteine residues in Igls may be important for the maintenance of their active conformations.

Confocal microscopy analysis demonstrated that the two Igls colocalized on the plasma membrane. However, it was also of interest that Ig1 and Ig2 showed different localization patterns in some intracellular vacuoles. This finding is in accord with the observation for *E. dispar* in a previous study using mouse MAbs specific for Ig1 and Ig2 of *E. dispar* (45). Recently, it has been reported that phagosomes of *E. histolytica* contain Ig1 and that the quantity of Ig1 varies during the maturation of the phagosome (35, 36). In addition, the expression level of the Ig1 gene is seven times higher than that of the Ig2 gene when the levels are compared by real-time PCR analysis (45). Although the primary structures of Ig1 and Ig2 are similar, these observations suggest that the two Igls may have different functions and different levels of expression during phagosome maturation, and the specific MAbs generated in this study may be useful for determining the associations of Ig1 and Ig2 with phagocytosis. We also note that different localization patterns of the two isotypes of the Rab7 small GTPase, *E. histolytica* Rab7A and *E. histolytica* Rab7B, in lysosomes and phagosomes have been reported previously (40).

We have generated several human MAb Fab fragments using combinatorial immunoglobulin gene libraries prepared from peripheral lymphocytes of a patient with an amebic liver abscess and asymptomatic cyst passers (8, 47, 52). Several Fabs recognize Hgl and are able to inhibit amebic adherence to host cells in vitro. However, we suspect that the in vivo effect of Fab fragments to *E. histolytica* trophozoites will be restricted because of the lack of an Fc region. Since the MAbs described in this paper are complete immunoglobulins, the effects of human MAbs on *E. histolytica* trophozoites in vivo may be induced with complement activation through the classical pathway (19). Indeed, it is well-known that IgM, in particular, is a mediator of complement activation. However, it has also been reported previously that Hgl of *E. histolytica* inhibits the assembly of C8 and C9 into the C5b-C9 membrane attack complex, thereby preventing complement-mediated lysis of the parasite (6). Recently, a cohort study in Bangladesh demonstrated that the mucosal IgA response directed to Hgl is linked to protection from both infection and disease (20, 21). In contrast, serum IgA has not been correlated with infection. Therefore, it is suggested that the systemic anti-Hgl antibody response may not offer direct protection from amebiasis (19). The details of the humoral immune response to Ig1 are unknown, but we have observed that serum antibodies to Ig1 are detected not only in symptomatic patients but also in asymptomatic *E. histolytica* cyst passers (46). In addition, sera from hamsters immunized with native Ig1 can inhibit in vitro amebic adherence to CHO cells by 98% at a 1:10 dilution (11).

In our previous study, the incidence of amebic liver abscess in hamsters was significantly reduced by pretreatment with 1 or 10 mg of mouse MAb EH3015, which belongs to the IgG1 family (12). In the present study, complete protection was detected only in 3 of 12 hamsters pretreated with 5 mg of XEhI-20, although a reduction of the mean abscess size was observed in all groups pretreated with one of the three adher-
ence-inhibiting human MAb to Igls. The difference in protective activity between the mouse and human MAb may depend on differences of subtype and avidity for hamster complement and effector cells. In a mouse model, the mechanisms through

FIG. 5. Localization of Ig1 and Ig2 on trophozoites of *E. histolytica* HM-1:IMSS observed by confocal laser scanning microscopy. Fixed trophozoites were stained with Alexa Fluor 488-labeled XEhl-20, specific for Ig1 (green) (A), and Alexa Fluor 594-labeled XEhl-B5, specific for Ig2 (red) (B). A differential interference contrast microscopy image is shown in panel C. A merged image of panels A and B is shown in panel D. The arrow and arrowhead indicate the individual localization patterns of Ig1 and Ig2, respectively. The bar indicates 10 μm.

FIG. 6. Effects of human MAb on adherence between *E. histolytica* and CHO cells. Trophozoites (10⁴) were pretreated with 10 μg of MAb. The rate of adherence is expressed as a percentage of the adherence seen with PBS-treated controls. The results are presented as means ± standard deviations of data from four experiments. Asterisks indicate *P* values of <0.0001 (for comparison with the PBS control), 0.0029 (for XEhl-20 versus XEhl-B5), 0.0212 (for XEhl-20 versus XEhl-H2), and 0.0284 (for XEhl-B5 versus XEhl-H2).

FIG. 7. Effects of human MAb on amebic liver abscess formation in hamsters. Each hamster received an intraperitoneal injection of 0.5 ml of PBS containing 5 mg of human MAb 24 h before intrahepatic inoculation with *E. histolytica* trophozoites. Control hamsters received 0.5 ml of PBS only or 0.5 ml of PBS containing 5 mg of human polyclonal IgG or IgM. Abscess size is expressed as a percentage of the size of the abscessed liver. Horizontal bars indicate the mean values for each group. Numbers in parentheses indicate the number of hamsters in each group. XEhl-20 versus IgG control, *P* < 0.0001; XEhl-B5 versus IgG control, *P* < 0.0001; XEhl-H2 versus IgM control, *P* = 0.0003.
which human *E. histolytica*-specific antibody may provide protection include the inhibition of amebic adherence to target cells, antibody-dependent cell-mediated cytotoxicity, and complement activation and lysis of trophozoites (43). It is probable that rodent Fc receptors have avidities similar to those of human immunoglobulin. However, the subtypes of MAbs described in this paper are IgG2 and IgM. Therefore, it is likely that hamster Fc receptors do not bind to the human MAbs, although complement activation may occur.

In the gene analysis of the heavy-chain variable region, the closest germ lines for the V and D segments of the four human MAbs were different, and an IgBLAST search for these MAbs did not identify any identical immunoglobulin genes in the database. XenoMouse mice contain approximately 2 Mb of the human immunoglobulin heavy and κ light chain loci, which functionally recapitulate the human humoral immune system (32). Analyses of human antibody transcripts from XenoMouse spleens and lymph nodes demonstrate that V, D, and J gene utilization patterns in nonimmunized animals are nearly identical to the gene utilization patterns reported for humans with extensive antigenic histories (16). In our previous study, analyses of heavy-chain genes for anti-Hgl human MAb Fab fragments revealed that all the closest germ lines for V segments belong to the VH3 family (52). In the present study, all the IgG2 MAbs also belonged to the VH3 family, and this finding appears to agree well with the proposal that VH3 antibodies are important for defense against a variety of viruses (2, 25) and bacteria (1, 44).

A high prevalence of *E. histolytica* infection in patients with human immunodeficiency virus (HIV) infection and AIDS in Japan and Taiwan has been reported recently (23, 24, 33). Higher rates of seropositivity for *E. histolytica* in HIV-infected patients than in non-HIV-infected patients with gastrointestinal symptoms in China have also been demonstrated previously (7). However, anti-*E. histolytica* antibodies have occasionally not been detected in AIDS patients with invasive amebiasis (34, 41). Extraintestinal amebiasis, and especially amebic liver abscess, is the major cause of high mortality from amebiasis, and therefore, passive immunization with the human MAbs reported in the present study may be applicable in immunoprophylaxis to prevent the development of invasive amebiasis in immunodeficient patients. The fully human MAbs to Igl5 may provide a new strategy for the control of amebiasis.

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