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United States Patent [19][11] **Patent Number:** **6,110,463****Riggs et al.**[45] **Date of Patent:** **Aug. 29, 2000**[54] **ANTI-CRYPTOSPORIDIUM PARVUM PREPARATIONS**[75] Inventors: **Michael W. Riggs**, Tucson, Ariz.;
Lance E. Perryman, Cary, N.C.[73] Assignees: **North Carolina State University**,
Raleigh, N.C.; **The Arizona Board of Regents**, Tucson, Ariz.[21] Appl. No.: **08/828,943**[22] Filed: **Mar. 27, 1997****Related U.S. Application Data**

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[51] **Int. Cl.**⁷ **A61K 39/395**; A61K 35/20;
C07K 16/20; C12N 5/20[52] **U.S. Cl.** **424/151.1**; 424/535; 424/807;
435/7.22; 435/70.21; 435/172.2; 435/342;
530/388.6; 530/822; 530/832[58] **Field of Search** 424/130.1, 151.1,
424/265.1, 266.1, 269.1, 535, 807; 435/7.22,
70.21, 172.2, 947, 342; 530/388.6, 389.1,
822, 832; 935/104, 107, 108[56] **References Cited****PUBLICATIONS**Riggs, M.W., Yount, P.A., Stone, A.L., Langer, R.C. (1996) Protective Monoclonal Antibodies Define a Distinct, Conserved Epitope on an Apical Complex Exoantigen of *Cryptosporidium parvum* Sporozoites. *J. Euk. Microbiol.* 43:74S-75S.Langer, R.C., Riggs, M.W. (1996) Neutralizing Monoclonal Antibody Protects Against *Cryptosporidium parvum* Infection by Inhibiting Sporozoite Attachment and Invasion. *J. Euk. Microbiol.* 43:76S-77S.Albert, M.M., Rusnak, J., Luther, M.F. and Graybill, J.R. (1994) Treatment of murine cryptosporidiosis with anti-cryptosporidial immune rat bile. *Am. J. Trop. Med. Hyg.*, 50:112.Arrowood, M.J., Mead, J.R., Mahrt, J.L. and Sterling, C.R. (1989) Effects of immune colostrum and orally administered ant sporozoite monoclonal antibodies on the outcome of *Cryptosporidium parvum* infections in neonatal mice. *Infect. Immun.*, 57:2283.Arrowood, M.J., Sterling, C.R. and Healey, M.C. (1991) Immunofluorescent microscopical visualization of trails left by gliding *Cryptosporidium parvum* sporozoites. *Parasitol.*, 77:315-317.Bjorneby, J.M. Riggs, M.W. and Perryman, L.E. (1990) *Cryptosporidium parvum* merozoites share neutralization-sensitive epitopes with sporozoites. *J. Immunol.*, 145:298-304.Bjorneby, J.M., Hunsaker, B.D., Riggs, M.W. and Perryman, L.E. (1991) Monoclonal antibody immunotherapy in nude mice persistently infected with *Cryptosporidium parvum*. *Infect. Immun.*, 59:1172.Bonnin, A., Dubremetz, J.F. and Camerlynck, P. (1991) Characterization of microneme antigens of *Cryptosporidium parvum*. *Infect. Immun.*, 59:1703.Bonnin, A., Dubremetz, J.F. and Camerlynck, P. (1993) A new antigen of *Cryptosporidium parvum* micronemes possessing epitopes cross-reactive with macrogamete granules. *Parasitol. Res.*, 79:8-14.Bonnin, A., Gut, J., Dubremetz, J.F., Newlson, R. and Camerlynck, P. (1995) Monoclonal antibodies identify a subset of dense granules in *Cryptosporidium parvum* zoites and gamonts. *J. Euk. Microbiol.*, 42:395.Borowitz, S.M. and Saulsbury, F.T. (1991) Treatment of chronic cryptosporidial infection with orally administered human serum immune globulin. *J. Pediatrics*, 119:593.Cama, V.A. and Sterling, C.R. (1991) Hyperimmune hens as a novel source of anti-Cryptosporidium antibodies suitable for passive immune transfer. *J. Protozool.*, 38:42S.Cho, M.-H. (1993) Passive transfer of immunity against *Cryptosporidium* infection in neonatal mice using monoclonal antibodies. *Kor. J. Parasitol.*, 31:223-30.Cochrane, A.H., Aikawa, M., Jeng, M. and Nussenzweig, R.S. (1976) Antibody-induced ultrastructural changes of malarial sporozoites. *J. Immunol.*, 116:859.Doyle, P.S., Crabb, J. and Petersen, C. (1993) Anti-*Cryptosporidium parvum* antibodies inhibit infectivity in vitro and in vivo. *Infect. Immun.*, 61:4079.Fayer, R., Perryman, L.E. and Riggs, M.W. (1989) Hyperimmune bovine colostrum neutralizes *Cryptosporidium* sporozoites and protects mice against oocyst challenge. *J. Parasitol.*, 75:151.Fayer, R., Andrews, C., Ungar, B.L.P. and Blagburn, B. (1989) Efficacy of hyperimmune bovine colostrum for prophylaxis of cryptosporidiosis in neonatal calves. *J. Parasitol.*, 75:393.Fayer, R., Guidry, A. and Blagburn, B.L. (1990) Immunotherapeutic efficacy of bovine colostrum immunoglobulins from a hyperimmunized cow against cryptosporidiosis in neonatal mice. *Infect. Immun.*, 58:2962.Fayer, R., Tilley, M., Upton, S.J., Guidry, A.J., Thayer, D.W., Hildreth, M. and Thomson, S. (1991) Production and preparation of hyperimmune bovine colostrum for passive immunotherapy of cryptosporidiosis. *J. Protozool.*, 38:38S.

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Primary Examiner—Christopher L. Chin*Assistant Examiner*—James L. Grun*Attorney, Agent, or Firm*—Oblon, Spivak, McClelland, Maier & Neustadt, P.C.[57] **ABSTRACT**Compositions and methods useful for conferring passive or active immunity to the parasite, *C. parvum*. A high molecular weight glycoprotein antigen isolated from *C. parvum*, capable of binding the mAb 3E2, was shown to harbor an epitope critical for triggering the neutralizing CSP-like reaction in the parasite. Antibodies targeted against the critical epitope were shown to possess neutralizing activity, and could be combined with other anti-*C. parvum* monoclonal antibodies and administered to an animal to confer passive immunity. Immunogenic compositions including the purified antigen are disclosed for use in stimulating an active immune response against *C. parvum*.**23 Claims, No Drawings**