Does the capsule component of the Cryptococcus neoformans glucuronoxylomannan impair transendothelial migration of leukocytes in patients with Cryptococcal meningitis? (letter)
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Reply

To the Editor—We commen e ha e commen s of Thompson [1], who kindly provided some da a as a supplement ary o our findings [2]. As originally s a ed, we failed o find an associa ion of serum reac ivi y wih clinical profiles, including pa ien age or sex or dura ion, si e, or number of molluscum lesions. Al hough Thompson did no repor a correla ion of he rela iven an imbody i er in heir ELISA sys em and clinical sympoms [3], we hink i should be no ed ha 1 of he weakly posi ve sera lacked reac ivi y wi h 33/35-kDa polypep ides [1]. These resul s sugges ha he ypes of an imbody may differ according o he reac ivi y measured by ELISA. Fur her longi udinal sudies wi h a large popul a ion is necessary o clarify he clinical significance of he wo ypes of an imbody.

Unfor una ely, we did no purify molluscum con agiosum virus (MCV) virions separa ely, since i was our purpose o ob ain a sufficien amoun of viral DNA o esablish a library. The ac ul propor ions of MCV sub ypes 1, 1v, and 2 in our pooled samples remains unknown. However, we hough ha mos of our samples consis ed of MCV 1v because a previous large epidemiologic sys em revealed ha sub ype 1v accoun ed for 96% of he s rains iso la ed in he Tokyo area [4], and we previously esablished a genomic library of MCV 1v [2]. I appears e ha he discrimin a e nor min differences in molecular masses when various iso la es are compared on he same polycrylamide gel. In addi ion, we do no hink i is appropri a e or os ima e he molecular masses of pro ions wi h ~70 and ~34 kDa on he same polycrylamide gel. Thomp- son [1] poin ed ou ha he size of larger an impent he ypes may have been underes ima ed (figures 1, 2, and 6 in [2]), which could be due o he use of higher percen age acrylamide. We repea edly performed elec rohoreses using gels a differen con cen ra ions and finally de ermined he molecular masses of he wo major an impent he ypes.

Oda e al. [5] analyzed he sue ural polypep ides of MCV by SDS-PAGE. He found ha only wo polypep ides, designa ed A and D, which were coinciden ally demons ra ed a o be wo major an imge pro ions [2], among seven major polypep ides differed in heir mobili y on acrylamide gel according o he iso la es. As- suming ha , as Thompson repor ed [1], he variabili y of he ypes of MCV DNA, i migh be immunologically impor an because MCV may have undergone changes in i surface pro ions during he evolu ionary process in response o he hos. However, i remains o be clarified why each of he polypep ides A and D is recognized as a wide, blurred band, ra her han wo discrete e bands, when pooled un yped MCV are analyzed on SDS-polyacrylamide gel [5]. We believe ha some unknown fac ors o her han sub ypes of MCV DNA par icipa e in he divergenc e of he wo an imgent polypep ides.

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Does the Capsule Component of the Cryptococcus neoformans Glucuronoxylomannan Impair Transepithelial Migration of Leukocytes in Patients with Cryptococcal meningitis?

To the Editor—The encapsula ed yeas -like fungus Cryptococcus neoformans is he leading cause of mycological infec ion of he cen ral nervous sys em in pa ien s wi h compromised cell-media ed immuni y [1]. Recen ly, we demons ra ed ha he cerebrospinal fluid (CSF) of pa ien s wi h cryp cococal meningi is is con a ins high levels of he neu rophil che moa rac he ne erlu in (IL)-8, despi e he fac ha he CSF con a ins few neu rophils [2]. The cryp cococal capsular polysaccharide glucuronoxylomannan (GXM) is presen in serum and CSF of pa ien s wi h cryp cococal meningi is, and GXM is known o he seeral wih he neu rophil migra ion [3]. We demons ra ed ha he GXM is capable of inducing he produc ion of IL-8 by brain cells, and i also preven s neu rophils from migra ion oward IL-8 [4]. Consequen ly, a high ra io of GXM in serum and CSF wi he CSF neu rophil cell coun s of 35 Du ch human immunodeficiency virus—infec ion pa ien s wi h a cul ure-pro ven diagnosis of cryp cococal meningi is is he ween 1986 and 1996. An igen i ers for he pa ien s were measured wi h com ercial ki s rou inel y used for diagnos is is ear apic cal cryp cococal an igen
Figure 1. Inverse correlation between radio of leukocyte count in cerebrospinal fluid (CSF) and cryptococcal glucuronoxylomannan in serum ([GXM]_{se}) over those in CSF ([GXM]_{csf}) in 35 patients with cryptococcal meningitis.

(mainly Murex Cryptococcus Test; Murex, Ken, UK) and were obtained within 5 days of the CSF leukocyte cell counts. Since GXM can a rac neurophils [4], he GXM concen ra ion gradient over he blood brain barrier (expressed as ra io of i ers in serum vs. CSF) is expec ed to be more cri ical o he CSF leukocy e cell coun than are absolue GXM concen ra ions. Figure 1 demon- stra es a rica signican inverse correla ion be ween he (log) GXM ra io and he (log) CSF leukocy e cell coun in pa -s wi h cryp- tococcus. (Correla ion coefficien of log values: $\rho = 0.54, n = 35$; wo-sided $P < .001$). These da a sugges ha he in vi ro finding of inTerence of GXM wi h neupol migra ion may indeed represen a pa hogenic mecianism in cryp ococcal meningi is.

References


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