Disruption of outer blood-retinal barrier by Toxoplasma gondii-infected monocytes is mediated by paracrinely activated FAK signaling

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Ocular toxoplasmosis is mediated by monocytes infected with Toxoplasma gondii that are disseminated to target organs. Although infected monocytes can easily access to outer blood-retinal barrier due to leaky choroidal vasculatures, not much is known about the effect of T. gondii-infected monocytes on outer blood-retinal barrier. We prepared human monocytes, THP-1, infected with T. gondii and human retinal pigment epithelial cells, ARPE-19, grown on transwells as an in vitro model of outer blood-retinal barrier. Exposure to infected monocytes resulted in disruption of tight junction protein, ZO-1, and decrease in transepithelial electrical resistance of retinal pigment epithelium. Supernatants alone separated from infected monocytes also decreased transepithelial electrical resistance and disrupted tight junction protein. Further investigation revealed that the supernatants could activate focal adhesion kinase (FAK) signaling in retinal pigment epithelium and the disruption was attenuated by FAK inhibitor. The disrupted barrier was partly restored by blocking CXCL8, a FAK activating factor secreted by infected monocytes. In this study, we demonstrated that monocytes infected with T. gondii can disrupt outer blood-retinal barrier, which is mediated by paracrinely activated FAK signaling. FAK signaling can be a target of therapeutic approach to prevent negative influence by infected monocytes on outer blood-retinal barrier.