

Reply to more on: the role of thrombin in gliomas

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See also Arbit E. More on: the role of thrombin in gliomas. This issue, p 286. Hua Y, Tang L, Keep RF, Schallert T, Fewel ME, Muraszko KM, Hoff JT, Xi G. The role of thrombin in gliomas. *J Thromb Haemost* 2005; **3**: 1917–23.

We thank Dr Arbit for his interest in our article. We have demonstrated that argatroban reduces peritumoral brain edema, tumor mass and improves tumor-induced neurological deficits in a rat glioma model [1,2]. As Dr Arbit suggests, argatroban may also be useful to reduce the deep vein thrombosis that can occur in glioma patients [3].

Argatroban is a small molecule that binds to the active site of thrombin [4]. Its size may facilitate its entry across the disrupted blood–brain barrier or blood–glioma barrier. Unlike heparin, argatroban is a direct thrombin inhibitor that does not require a cofactor to inhibit thrombin. Argatroban has a lower hemorrhagic potential *in vivo* than other thrombin inhibitors such as heparin or hirudin [4]. In a previous study, we found that argatroban reduces brain edema induced by intracerebral hemorrhage and does not exacerbate hemorrhage in rats [5].

As noted by Dr Arbit, one of the disadvantages of using argatroban is that it should be administered intravenously. Melagatran is another low molecule direct thrombin inhibitor. It can be administered orally in the form of a pro-drug, ximelaga-

tran, which is rapidly converted to the active molecule [6]. As Dr Arbit suggests, it will be very important to determine whether ximelagatran/melagatran will also be effective in glioma treatment.

References

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