Kinetics of Proteins in the Blood-Brain Barrier

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Abstract

The delivery of chemotherapy for cancer into the central nervous system, in particular the brain, remains a challenge. This results in brain metastases commonly being a cause of death from cancer. Here, we look at the environment of the blood-brain barrier. Then, we explore two proteins (breast cancer resistance protein and p-glycoprotein) that may inhibit the transport of medications (erlotinib and flavopiridol) across the blood-brain barrier. Next, we look at a mathematical model to quantify the effect of these two efflux-inducing proteins on transport. Last, I create a model using the COMSOL Multiphysics® software to describe and predict behavior at the blood-brain barrier (BBB) with respect to one of the chemotherapeutic agents (erlotinib).

Reference

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Figures used in the abstract

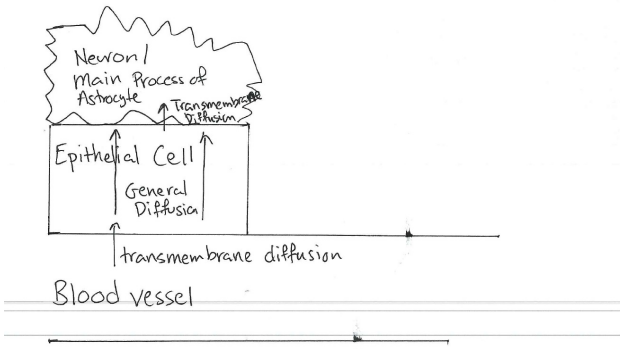

Figure 1

Figure 4. Dimensionless plot of erlotinib distribution as function of time in hcrp knock-out, R=1.28. A starting concentration of .125mol/cubic meter was used, as this is on the order of concentration of erlotinib in the blood of treated patients (). Top Left: t=0. Top Right: t=1. Bottom Left: t=10. Bottom Right: t=100. Bottom rectangle in each plot represents the concentration in the blood vessel, middle the epithelial cell, the top geometry the astrocyte.

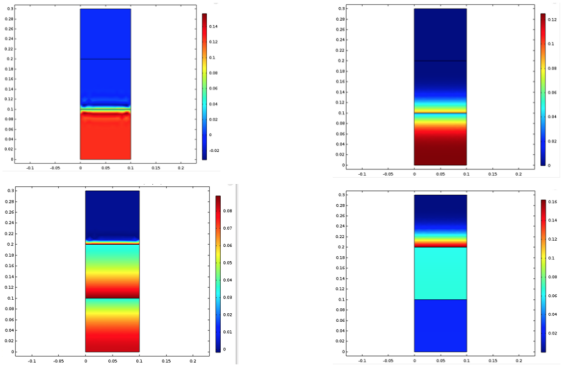

Figure 2

Figure 3. Dimensionless plot of erlotinib distribution as function of time in wildtype, R=1. A starting concentration of .125mol/cubic meter was used, as this is on the order of concentration of erlotinib in the blood of treated patients (). Top Left: t=0. Top Right: t=1. Bottom Left: t=10. Bottom Right: t=100.

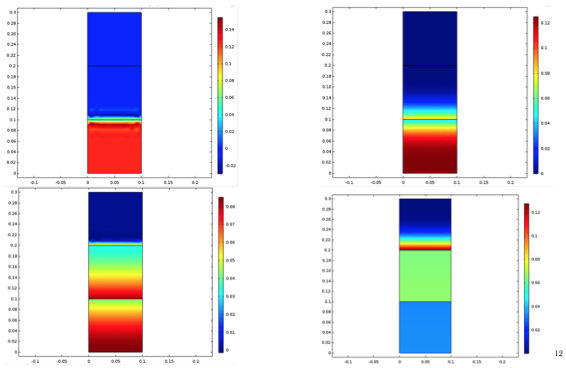

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Figure 3

Figure 6. Dimensionless plot of erlotinib distribution as function of time in bcrp and p-gy double knock-out, R=8.52. A starting concentration of .125mol/cubic meter was used, as this is on the order of concentration of erlotinib in the blood of treated patients ( ). Top Left: t=0. Top Right: t=1. Bottom Left: t=10. Bottom Right: t=100. Bottom rectangle in each plot represents the concentration in the blood vessel, middle rectangle the epithelial cell, the top geometry the astrocyte.

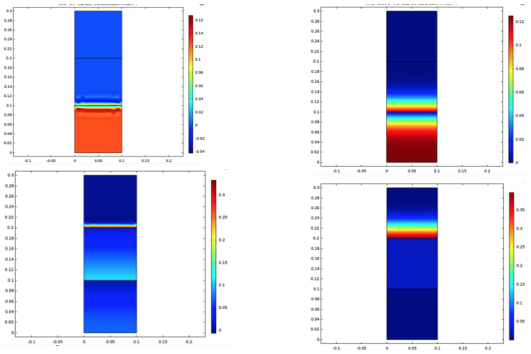

Figure 4