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A mathematical model simulation for tumor and organ uptake of 64Cu labelled amatuximab, an anti-mesothelin antibody by PET image and biodistribution

Jae-Ho Lee, Heejung Kim, Byungkook Lee and **Chang H Paik**
National Institutes of Health Clinical Center, USA

Objectives: To investigate the effect of the antibody dose and tumor size on tumor and organ uptake of 64Cu-amatuximab by mathematical model simulation and to develop a mathematical model simulator to predict biodistribution in a shed antigen tumor model

Methods: A mathematical model simulator using Matlab has been developed by solving ODE to predict the dose effect of the antibody, the biodistribution (BD), and PET imaging in mesothelin shed tumor model based on previous experimental data. Previously, PET imaging and BD of 64Cu-amatuximab was studied to investigate tumor and organ uptake of 64Cu labelled amatuximab in groups of nude mice (n=5) with mesothelin-expressing A431/H9 tumors by co-injecting cold amatuximab and 64Cu-amatuximab.

Results: This mathematical model simulator was developed to accommodate co-injection of cold amatuximab and 64Cu-amatuximab. A previous mathematical model to predict antibody injection in mesothelin shed tumor model has only a feature to predict dose effect of radiolabeled antibody in tumor cells. In this model simulator, amount of tumor cells, amatuximab (mAb) bound, radiolabeled mAb bound tumor cells were predicted as tumor growing. Also, the distribution of 64Cu-amatuximab in mice can be predicted by adopting PET imaging and BD analysis at different time points that were published in our previous study. Shed mesothelin effects also have been considered depending on dose of mAb and pharmacokinetic parameters have been fitted to predict experimental data.

Conclusions: This mathematical model simulator provides deep insights on tumor uptake and retention of the radiolabeled antibody in tumor and organ and potentially can give quantitative information on the optimum injected dose to maximize the tumor uptake.

leejaeho@cc.nih.gov

Browning of the white adipose tissue and metabolic dysfunction in cancer associated cachexia

Michele Petruzzelli
Cambridge University School of Medicine, UK

Human cancer develops as a localized focus of uncontrolled cell growth and subsequently progresses into systemic disease. Cancer research primarily focuses on the agents, events, and genetic alterations underlying tumor initiation, progression and metastasis. However, many cancer patients die because of cachexia, a systemic wasting disease caused by the tumor, but manifested by alterations in distant organs resulting in weight loss, fatigue, anemia, progressive atrophy of the white adipose tissue (WAT) and skeletal muscle. Systemic inflammation and metabolic dysfunction have been proposed as the major culprits in cachexia pathophysiology, but their chronological appearance and regulation remain elusive. We have recently shown that during the clinical progression of cancer, inflammatory mediators trigger a phenotypic switch from WAT to brown adipose tissue (BAT), a phenomenon termed WAT-browning, which is functionally responsible for increased lipid mobilization and energy consumption. WAT-browning contributes to the metabolic dysfunction observed in cancer and leads to the wasting syndrome. Current investigation focuses on the cellular players and molecular events that drive the inflammatory response during cachexia.

MP753@cam.ac.uk