Preparation and Evaluation of Lactosylated Albumin Nanoparticle Containing Doxorubicin and Paclitaxel for Treating Hepatocellular Carcinoma
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**Purpose**
Lactose residue is a promising liver asialoglycoprotein receptors (ASGPR). Herein, we introduce doxorubicin and paclitaxel co-bound lactosylated albumin (Lac-BSA) nanoparticles (Dox/Pac Lac-BSA NPs) with good liver targetability.

**Methods**
Lac-BSA was synthesized by conjugating lactobionic acid to naïve BSA then characterized by mass spectrometry. Dox/Pac Lac-BSA NPs were fabricated utilizing high-pressure homogenization and evaporation with Nab® (nanoparticle albumin bound) technology.

**Results**
Dox/Pac Lac-BSA NPs were spherical and well-dispersed, with a 148.7±13.8nm particle size and -54.1±0.7mV zeta potential at a 100% Lac-BSA feed ratio. Combined Dox and Pac synergistic cytotoxicity was confirmed in Hep G2 cells. Specifically, the inhibitory concentration (IC50; 0.21±0.02μg/ml) for Dox/Pac Lac-BSA NPs was 3.2 time lower than plain Dox/Pac BSA NPs (IC50; 0.68±0.04μg/ml). Also, Dox/Pac Lac-BSA NPs exhibited better internalizing in Hep G2 cells (61.8% vs. 14.4% for Dox) and spheroids compared to Dox/Pac BSA NPs.

**Conclusion**
Dox/Pac Lac-BSA NPs displayed much greater localization into ICR mice livers compared to Dox/Pac BSA NPs. This was indicated by the presence of NP lactose residues revealed by a galactose inhibition study. Based on these results, we believe that lactose-modified albumin-based nanoparticles fabricated with the Nab® technique can be a good prototype delivery platform for treating HCC via hepatocyte targeting.