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Doxorubicin conjugated Poly (lactic-co-glycolic acid)/Poly (styrene-alt-maleic anhydride) Core/Shell Microparticles for MT1-MMP targeting of Hepatic cancer

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Research: In this study, we demonstrated that the MT1-MMP-responsive peptide (sequence: GPLPLRSWGLK) and doxorubicin-conjugated Poly (lactic-co-glycolic acid)/poly (styrene-alt-maleic anhydride) core/shell microparticles (PLGA/pSMA MPs) can be applied for intrahepatic arterial injection for hepatocellular carcinoma (HCC). PLGA/pSMAMPs were prepared with a capillary-focused microfluidic device.

Results: The particle size, observed by scanning electron microscopy (SEM), was around 22± 3μm. MT1-MMP-responsive peptide and doxorubicin (DOX) were chemically conjugated with pSMA segments on the shell of MPs to form a PLGA/ pSMA-peptide-DOX complex, resulting in high encapsulation efficiency (91.1 %) and loading content (2.9 %). DOX was released from PLGA/ pSMA-peptide-DOX MPs in a pH-dependent manner (~25 % at pH 5.4 and ~8 % at pH 7.4) and accumulated significantly in an MT1-MMP-over-expressing Hep3B cell line. An*in vivo* intrahepatic injection study showed localization of MPs on the hepatic vessels and hepatic lobes up to 24 hrs after the injection without any shunting to the lung. Moreover, MPs efficiently inhibited tumor growth of Hep3B hepatic tumor xenografted mouse models.

Conclusion: Size-controlled PLGA/pSMA core−shell MPs were successfully produced by using a microfluidic technique. Synthesized MPs were conjugated with DOX, and the MT1-MMP-targeting peptide was introduced as a linker molecule between DOX and MPs to enhance tumor targeting. These MPs showed pH-sensitive sustained drug release for one month. Moreover, in vitro and in vivo release studies of MPs demonstrated that DOX released from PLGA/pSMA-peptide-DOX MPs has more efficient cellular entry into Hep3B cells and improved tumor suppression compared to PLGA/pSMADOXMPs. These results suggest that this material can be deployable as a potential candidate for TACE therapy for HCC.

Biography:

Junghan Lee is presently a research Professor of Department of New Drug Development at Inha University School of Medicine. In 2011, a Ph.D. in Molecular Medicine was conferred on him by Ajou University School of Medicine. During the Ph.D. course, he also participated in Institute Pasteur as a co-researcher. From 2011-2012, he was a Visiting Postdoctoral Associate of Department of Chemistry at the College of Arts and Sciences in Florida International University. During his Ph.D. program and Post-Doc, he was involved in numerous publications relating to Nano/Bio Chemistry. He has been participating in many research projects associated with “Development of novel nanoprobes for the bio imaging and cancer diagnostics” and now continuously studying for related research.