Commentary
Volume 8:S5, 2024

Virology: Current Research

ISSN: 2736-657X Open Access

Next-Generation Imaging and Drug-Delivery System with a Mucosal Capsid Platform

Naresh N Dhanasekar and R Holland Cheng*

Department of Molecular and Cellular Biology, University of California, Davis, USA

About the Study

The development of smart carriers for drug delivery has significantly benefited from recent developments in nanotechnology. In particular, Virus-Like Particles (VLP) have gained tremendous attention for offering a variable framework for drug encapsulation [1]. Besides drug delivery, VLPs contribute to many applications, including gene therapy, vaccine development, theranostic agents, cancer treatment and Positron Emission Tomography (PET) imaging [2-6]. VLPs are simple protein capsids whose structure is engineered to void the typical viral genome for viral replication. Similarly, the design of Hepatitis E Nanoparticles (HEVNP) conjugated with the positron-emitting radionuclide ^{68}Ga (Gallium) could enable targeted delivery of drugs and enhanced diagnostic capabilities through PET imaging. By utilizing the unique properties of ^{68}Ga-conjugated HEVNP, this research aims to develop a various platform for targeted drug delivery and improved diagnostics, potentially significantly impacting the management of various diseases.

As reported in molecular pharmaceutics, Lambidis and colleagues have taken a critical step in utilizing HEVNP as liver-specific vehicles [6]. The cush feature makes them harmless and biocompatible under physiological conditions, where HEVNP contributed significantly to the field of theranostics and drug delivery [7]. Additionally, the epitome destruction of the engineered viral particles was less identified by the floating antibodies against viral capsids and the pharmaceutical industry utilized the phenomenal behavior of HEVNP in the production of vaccines [8]. Replacing traditional diagnostic radionuclides with alternative isotopes that emit different types of radiation can convert imaging tracers into potent and targeted molecular therapies. In this context, developing a ^{68}Ga-conjugated HEVNP holds promise for targeted drug delivery and diagnostic applications using PET. The authors used the chemical stability of the HEVNP to be visualized *ex vivo* through PET. To be used as a liver carrier, the authors initially modified the surface of HEVNP with (^{68}Ga)-Dodecane Tetra Acetic Acid (DOTA) through covalent bond formation between the primary amine of the amino acid lysine and the NHS ester of the DOTA molecule. The structural properties of the HEVNP were not altered, as the authors confirmed them through cryo-electron microscopy assessment. To further throw light on the radioactivity of the modified HEVNP, the authors purified complex particle, (^{68}Ga)-DOTA–HEVNP, exhibited a higher radiolabeled yield of ~98% as compared to native HEVNP with only 0.2%.

Understanding the challenge underlying *in vivo* conditions, the authors performed *ex vivo* protocol to demonstrate the uptake of gallium-modified HEVNP through intravenous administration in healthy mice [9]. *Ex vivo* experiments revealed HEVNPs are superior to other VLPs in their absorption by the liver (~97% ID/g) followed by spleen (~18% ID/g) than the pancreas, kidney, lung, heart, stomach and intestinal regions. Furthermore, *in vitro* experiments with cell lines specific for macrophages (RAW 264.7) and Hepatocytes (Hep G2) revealed higher uptake of HEVNP, which was strongly associated with clathrin-mediated endocytosis. Clathirin-mediated endocytosis is a significant biological process adopted by cancer cells for internalization. Further, to prove this effect of HEVNP in cancer cells, the authors used colorectal cancer cell lines, HCT116 for their internalization experiments [10-12]. HCT116 cells adopted a step-wise gradient absorption of HEVNP from <1% to >6% within a short period, thus confirming the internalization property of HEVNP.

Molecular imaging has emerged as a powerful tool for the noninvasive visualization and quantification of biological processes at the cellular and molecular levels [13]. Radionuclide imaging techniques like PET have become increasingly valuable in drug development [14]. Improvements in surface modification with different chemical/physical strategies are of great value to investigate. Such modifications could lead to the delivery of several drugs attached to a single HEVNP. The creation of such stable drug delivery vehicles could orchestrate drug delivery or be expensive and tedious to perform *in vivo*. While organic and inorganic-based nanoparticles have potential toxicological concerns, HEVNP, being biocompatible, overcomes such limitations to exhibit little or no physiological concern with noninvasive mucosa-homing attributes [12]. Further, implementing a water-borne viral capsid demonstrates how HEVNP could lead to noninvasive means of diagnosis and therapeutics. These methods enable quantifying radiolabeled pharmaceutical formulations' *in vivo* distribution and kinetics, allowing for a direct correlation between pharmacological effects and the precise drug delivery site. Further advances in nuclear medicine have expanded the range of molecular radiotherapies, enabling the application of targeted treatments across a broad spectrum of diseases with the

***Address for Correspondence:** R Holland Cheng, Department of Molecular and Cellular Biology, University of California, Davis, USA; E-mail: rhch@ucdavis.edu*

Received date: 19-Jul-2024, Manuscript No. VCRH-24-141987; **Editor assigned:** 22-Jul-2024, Pre QC No. VCRH-24-141987 (PQ); **Reviewed:** 05-Aug-2024, QC No. VCRH-24-141987; **Revised:** 12-Aug-2024, Manuscript No. VCRH-24-141987 (R); **Published date:** 19-Aug-2024, DOI: 10.37421/2736-657X.2024.S5.004

recently added HEVNP platforms, as demonstrated by Lambidis and colleagues [6,9,11,15].

Acknowledgement

Juselius Foundation, National Institute of Health (TR002866, CA198880, CA225266 and EB021230), National Institute Food Agricul-ture (nos. CADMCB-7399-H), FiDiPro and University of California (UC) Science Translation and Innovative Research (STAIR) programs.

References

1. Segel, Michael, Blake Lash, Jingwei Song and Alim Ladha, et al. "Mammalian Retrovirus-like Protein PEG10 Packages its Own mRNA and can be Pseudotyped for mRNA Delivery." *Science* 373(2021):882-889.
2. Gee, Peter, Mandy SY Lung, Yuya Okuzaki and Noriko Sasakawa, et al. "Extracellular Nanovesicles for Packaging of CRISPR-Cas9 Protein and sgRNA to Induce Therapeutic Exon Skipping." *Nat Commun* 11(2020):1334.
3. Jariyapong, Pitchanee, Li Xing, Nienke E van Houten and Tian-Cheng Li, et al. "Chimeric Hepatitis E Virus-like Particle as a Carrier for Oral Delivery." *Vaccine* 31(2013):417-424.
4. Chen, Chun-Chieh, Marie Stark, Mo A Baikoghli and R Holland Cheng. "Hepatitis E Virus Nanoparticle Encapsulating Nano-Theranostic Reagent as Modularized Capsule." *Adv Res Gastroenterol Hepatol* 5(2017):555-674.
5. Ashley, Carlee E, Eric C Carnes, Genevieve K Phillips and Paul N Durfee, et al. "Cell-Specific Delivery of Diverse Cargos by Bacteriophage MS2 Virus-Like Particles." *ACS Nano* 5(2011):5729-5745.
6. Lambidis, Elisavet, Chun-Chieh Chen, Mo Baikoghli and Surachet Imlimthan, et al. "Development of ^{68}Ga-labeled Hepatitis E Virus Nanoparticles for Targeted Drug Delivery and Diagnostics with PET." *Mol Pharmaceutics* 19(2022):2971–2979.
7. Kamita, Shizuo G, Mo A Baikoghli, Luis Mde la Maza and R Holland Cheng. "Noninvasive, Orally Stable, Mucosa-Penetrating Polyvalent Vaccine Platform Based on Hepatitis E Virus Nanoparticle." In: Synthetic Biology–New Interdisciplinary Science. *IntechOpen* 2020.
8. Chen, Chun-Chieh, Li Xing, Marie Stark and Tingwei Ou, et al. "Chemically Activatable Viral Capsid Functionalized for Cancer Targeting." *Nanomedicine* 11(2016):377–390.
9. Lambidis, Elisavet, Dave Lumén, Elina Koskipahta and Surachet Imlimthan, et al. "Synthesis and *Ex vivo* Biodistribution of Two ^{68}Ga-Labeled Tetrazine Tracers: Comparison of Pharmacokinetics." *Nuclear Med Biol* 114(2022):151-161.
10. Huang, Tung-Yung, Tung-Cheng Chang, Yu-Tang Chin and Yi-Shin Pan, et al. "NDAT Targets PI3K-Mediated PD-L1 Upregulation to Reduce Proliferation in Gefitinib-Resistant Colorectal Cancer." *Cells* 9(2020):1830.
11. Lambidis, Elisavet, Chun-Chieh Chen, Dave Lumen and Ana Isabel Fraguas Sánchez, et al. "Biological Evaluation of Integrin $\alpha 3\beta 1$-Targeted ^{68}Ga-Labeled HEVNPs in HCT 116 Colorectal Tumor-Bearing Mice." *Eur J Pharm Sci* 180 (2023):106336.
12. Cheng, Tsai-Mu, Hsiu-Yi Chu, Haw-Ming Huang and Zi-Lin Li, et al. "Toxicologic Concerns with Current Medical Nanoparticles." *Int J Mol Sci* 23(2022):7597.
13. Krajcovicova, Sona, Andrea Daniskova, Katerina Bendova and Zbynek Novy, et al. "(^{68}Ga) Ga-DFO-c(RGDyK): Synthesis and Evaluation of Its Potential for Tumor Imaging in Mice." *Int J Mol Sci* 22(2021):7391.
14. Perkins, Alan C and Malcolm Frier. "Radionuclide Imaging in Drug Development." *Curr Pharm Des* 10(2004):2907-2921.
15. Hacker, Marcus, Thomas Beyer, Richard P Baum and Antonis Kalemis, et al. "Nuclear Medicine Innovations Help (Drive) Healthcare (Benefits)." *Eur J Nucl Med Mol Imaging* 42(2014):173-175.

How to cite this article: Dhanasekar, Naresh N and R Holland Cheng. "Next-Generation Imaging and Drug-Delivery System with a Mucosal Capsid Platform." *Virol Curr Res* 8(2024):004.