Yoko Matsumoto, Arch Cancer Res 2018, Volume 6
DOI: 10.21767/2254-6081-C4-014

Therapeutic effects of cationic liposomes against colon carcinoma along with apoptosis

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We have produced three-component cationic liposomes (CL) composed of 87 mol% L-α-dimyristoylphosphatidylcholine, 5 mol% polyoxyethylene (21) dodecyl ether and 8 mol% O,O'-ditetradecanoyl-N-(α–trimethylammonioacetyl) diethanolamine chloride, which were effective for inhibiting the growth of colorectal cancer (CRC) cells without using drugs. Fusion and accumulation of CL including the fluorescent probe in CRC cells was observed using confocal laser microscope without affecting normal cells. This result suggests that CL selectively fused and accumulated into CRC cell membrane, which overexpressed negativelly charged sialic acid-containing glycosphingolipids. The induction of apoptosis for CRC cells treated with CL was observed using TUNEL method. Apoptotic DNA rates in CRC cells treated with CL increased and a high apoptotic DNA rate was attained. We observed activation of caspase-3, -8 and -9 and decrease in mitochondrial transmembrane potential in CRC cells treated with CL, indicating that apoptotic signal passed through caspase-3, -8 and -9 and mitochondria. Therapeutic effects of CL on xenograft and hepatic metastasis mouse model of CRC *in vivo* were obtained. Remarkable reduction of tumor volume was obtained in xenograft model mice of CRC intravenously treated with CL. Many apoptotic cells in tissue section of tumor in xenograft mice treated with CL were observed. Relative liver weight of hepatic metastasis mouse model decreased after the treatment with CL. Reduction of tumor in the liver of hepatic metastasis mouse model was observed. The reduction of metastatic nodules was observed in the liver using HE staining method. Induction of apoptosis in metastasis mouse model was observed using TUNEL method. CL had no side-effects in the safety tests intravenously administered *in vivo*. The results of this study could be potentially advantageous for future clinical application of CL therapy in patients with CRC.

Recent Publications

1. Ichihara H, Motomura M and Matsumoto Y (2016) Negatively charged cell membrane-targeted highly selective chemotherapy with cationic liposomes against colorectal cancer *in vitro* and *in vivo*. Journal of carcinogenesis and mutagenesis 7:267-375.
2. Ichihara H, Okumura M and Matsumoto Y (2016) Therapeutic effects of hybrid liposomes against xenograft mouse model of colorectal cancer *in vivo* due to long term accumulation. Anticancer research 36(11):5875-5882.
3. Ichihara H, Kuwabara K and Matsumoto Y (2017) Trehalose liposomes suppress the growth of tumor on human lung carcinoma bearing mice by induction of apoptosis *in vivo*. Anticancer research 37(11):6133-6139.
4. Motomura M, Ichihara H and Matsumoto Y (2018) Nano-chemotherapy using cationic liposomes that strategically targets the cell membrane potential of pancreatic cancer cells with negative charge. Bioorganic & medicinal chemistry letters 28(7):1161-1165.
5. Okumura M, Ichihara H and Matsumoto Y (2018) Hybrid liposomes showing enhanced accumulation in tumors as therapeutic agents in the orthotopic graft model mouse of colorectal cancer. Drug delivery 25(1):1192-1199.

Biography

Yoko Matsumoto is a Professor in the Department of Life Sciences at Sojo University, Japan. She has completed her PhD in Pharmacy at Kyushu University, Japan. She was a Visiting Researcher at Colorado University in Boulder with Prof. Tom Cech. She has received Outstanding Female Researcher Award from the Society of Chemical Engineering, Japan. She is a Member of the Board for Japan Nanomedicine Society and Councilor for Japanese Association for Molecular Target Therapy of Cancer. Her current research interest focuses on "Liposomes for therapeutic applications". She has published more than 130 original papers.

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