

## **Biodegradable long-term sustained release microspheres including siRNA for tumor therapy**

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Recently, nucleic acid drugs have investigated as therapeutic tools of future generation. Particularly, the small interfering RNA (siRNA) has been known for its high gene silencing effect. Angiogenesis is important for the tumor growth and mainly induced by a vascular endothelial growth factor (VEGF). The angiogenesis could be suppressed by inhibiting the VEGF production using anti-VEGF siRNA in early phase of tumor formation. We have already reported that the gene silencing effect of siRNA was transient when siRNA soln. was administrated to mice bearing tumor cells by single intra-tumor injection. Therefore, the effective and sustained delivery system was required for siRNA. Our objective is to prepare the long-lasting release microspheres encapsulating siRNA in biodegradable polymer such as poly (lactic/glycolic acid) (PLGA) by w/o/w in water drying method. Mean particle diameter of obtained microspheres is around 40  $\mu\text{m}$  which is injectable size. The microspheres showed high encapsulation efficiency of siRNA when the anti-VEGF siRNA encapsulated with cationic carrier. *In vitro* release study, the siRNA was released sustainably from the microspheres for one month. *In vivo* study, tumor growth was continuously suppressed for one month by intra-tumor injection of microspheres including anti-VEGF siRNA into mice bearing tumor cells. Additionally, the microspheres encapsulating two kinds of siRNA which are for anti-VEGF and anti-apoptosis factor showed greater anti-tumor effect. The siRNA microspheres is currently being investigated for brain tumor therapy. The biodegradable long-lasting release microspheres of siRNA in this study is useful gene delivery system for not only cancer therapy but it could be also available for other disease such as viral disease.