Spotlight

By Anne Forde

Synthetic siRNA hampers Ewing sarcoma

Takigami *et al.*
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Ewing sarcoma is the second most common malignant bone tumor that mainly affects children and young adults. Of the Ewing sarcomas, 85% display a fusion gene – EWS/Fli-1 – which is a product of chromosomal translocation. The EWS fusion gene is thought to play a significant role in tumorigenesis and it has been reported that tumorigenesis of Ewing sarcoma cell lines can be reduced by antagonizing the gene.

In this study, Takigami *et al.,* created a chemically synthesized siRNA system to block EWS fusion protein. Two siRNA were generated: both targeted a specific form of EWS fusion gene, but one also possessed the aromatic compound pyridine at the 3' end. The siRNAs reduced EWS fusion protein in Ewing sarcoma cell lines that expressed that specific form of gene product. siRNA induced knockdown of EWS fusion protein correlated with decreased proliferation of the sarcoma cell lines but did not affect the viability of the cells as monitored by apoptosis.

In vivo, tumor growth was significantly suppressed in Ewing sarcoma tumor-bearing mice injected with the siRNAs. Importantly, the animals did not show any adverse effects of the siRNA treatment. The siRNA that included the aromatic compound performed more stably *in vivo.*

This study nicely demonstrates that synthetic siRNAs specific for EWS fusion can reduce expression of the protein and can inhibit the growth of Ewing sarcoma tumors *in vivo*. The siRNA version with an aromatic compound, in particular, offered stability without adverse side effects.

Inhibition of Ewing Sarcoma tumors in BALB/c nude mice with synthetic siRNAs targeting the EWS fusion gene: siEFp (siRNA with an aromatic compound pyridine at the 3' end), siEF (not modified at 3' end), siCONT (control siRNA) and PBS. The frequency at which the siRNAs were given to the animals is indicated by arrows.