LNA-mediated microRNA Silencing In Non-human Primates

Mar. 26th 2008 LNA-mediated microRNA silencing in non-human primates has been published in the March 26, 2008 online edition of *Nature*. The study authors, led by Dr Sakari Kauppinen, Director of MicroRNA Research at Santaris Pharma and visiting Professor at Wilhelm Johannsen Centre for Functional Genome Research, University of Copenhagen, used a high-affinity Locked Nucleic Acid-modified oligonucleotide (LNA-antimiR) to antagonize the liver-expressed microRNA-122 (miR-122) in rodents and non-human primates. Acute administration of the LNA-antimiR resulted in uptake of the compound in liver cells and formation of stable hetero duplexes between the LNA-antimiR and miR-122. This was accompanied by depletion of mature miR-122 and dose-dependent lowering of plasma cholesterol. Efficient silencing of miR-122 was achieved in primates by three intravenous doses of 3 mg/kg. The paper is the first demonstration of microRNA silencing in non-human primates. “We are excited by the results from this study, which demonstrate the great promise that LNA technology holds for targeting microRNAs and exploring their function in vivo,” said Sakari Kauppinen. “In the study, we used a simple intravenous delivery of an unconjugated LNA-antimiR to antagonize the liver-expressed microRNA-122 in African green monkeys, which resulted in long-lasting, efficient and reversible decrease in total plasma cholesterol without any evidence of adverse reactions.” “Even though further studies will be needed to optimize the dosing regimen and to assess the safety of LNA-antimiR compounds after long-term treatment, our findings represent an important step towards the development of LNA-based microRNA therapeutics,” said Kauppinen. Santaris Pharma is preparing to advance its first LNA-antimiR compound, targeting miR-122, into human clinical testing in the first half of 2008. The first trial will be a Phase I safety and pharmacokinetik study in healthy volunteers. The primate study was carried out in collaboration with the Connecticut based biotech company RxGen at the St. Kitts Biomedical Research Foundation. Source: Santaris Pharma

Source URL (retrieved on 05/03/2016 - 5:15pm):