EXIQON
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LNA™ antisense oligonucleotides for RNA therapeutics

- Successful in clinical research trials*
- Expert bioinformatics design service
- *In vivo* grade mg – kg scales
- Exceptional potency and biostability

In vivo Antisense LNA™ GapmeRs

Potent silencing of any of mRNA or lncRNA *in vivo*

exiqon.com/gapmer

In vivo miRCURY LNA™ microRNA Inhibitors

Potent microRNA inhibition *in vivo*

exiqon.com/in-vivo-mirna-inhibitors

In vivo miRCURY LNA™ microRNA Target Site Blockers

Identify microRNA targets *in vivo*

exiqon.com/mirna-target-site-blocker

*Phase II trials of LNA™ miR-122 inhibitor (Janssen et al., N Engl J Med., 2013).

Potent gene silencing *in vivo*

Therapeutic applications

With demonstrated excellent PK/PD properties and long-lasting activity *in vivo*, antisense technology is becoming the third major modality in the drug development industry.

Exiqon's third generation LNA™ antisense oligonucleotides enable silencing of messenger RNA, long non-coding RNA and microRNA in a broad range of tissues in animal models. We provide expert LNA™ antisense oligonucleotide design for therapeutic use.

Advanced design algorithms

Exiqon's sophisticated design algorithms minimize the screening required to identify highly potent and specific antisense oligonucleotides.

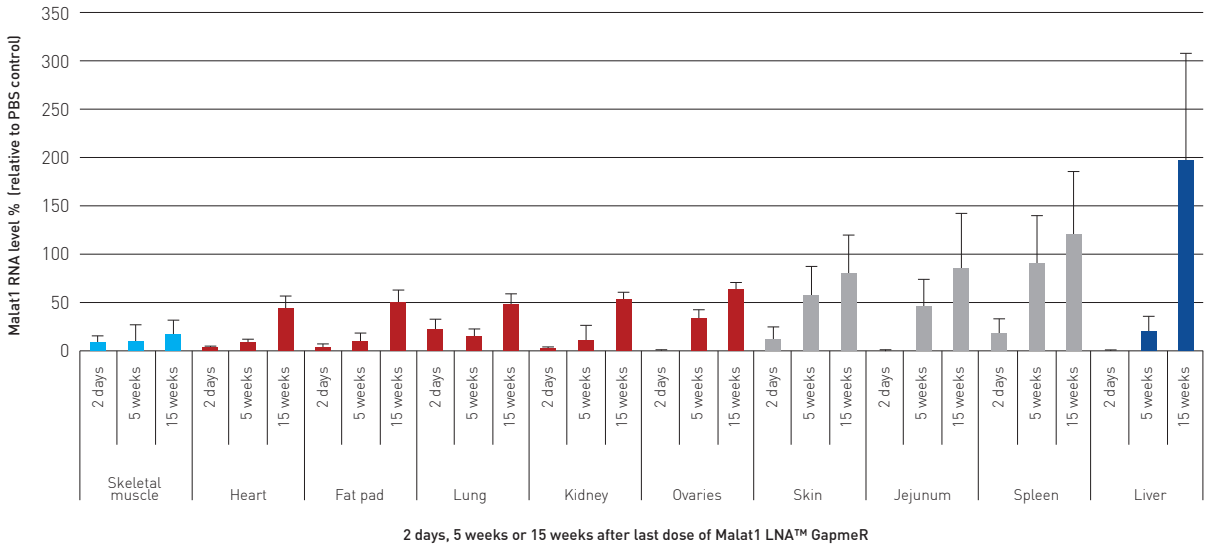
In vivo oligonucleotide synthesis

We supply highly purified LNA™ antisense oligonucleotides in mg – kg amounts for animal studies and clinical research.

In vivo Antisense LNA™ GapmeRs

- RNase H1-mediated silencing of mRNA and lncRNA
- Superior serum stability and biodistribution
- Active *in vivo* without formulation

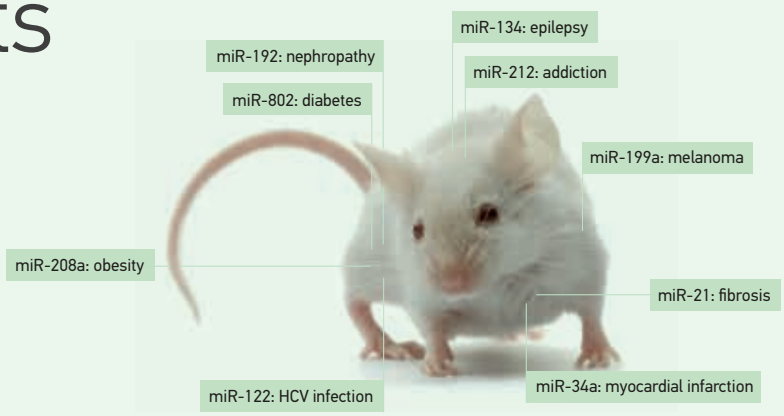
Potent and long lasting RNA silencing in a broad range of tissues



Antisense LNA™ GapmeR for knockdown of Malat1 lncRNA in mice was injected subcutaneously over a period of 4 weeks. Samples from a broad range of tissues from the mice were collected up to 15 weeks after last LNA™ GapmeR administration.

> ***"Tumor growth was significantly inhibited in mice injected with the SAMMSON-targeting Antisense LNA™ GapmeRs."***
>
> Prof. Jean-Christophe Marine, K.U. Leuven

Explore microRNA as therapeutic targets



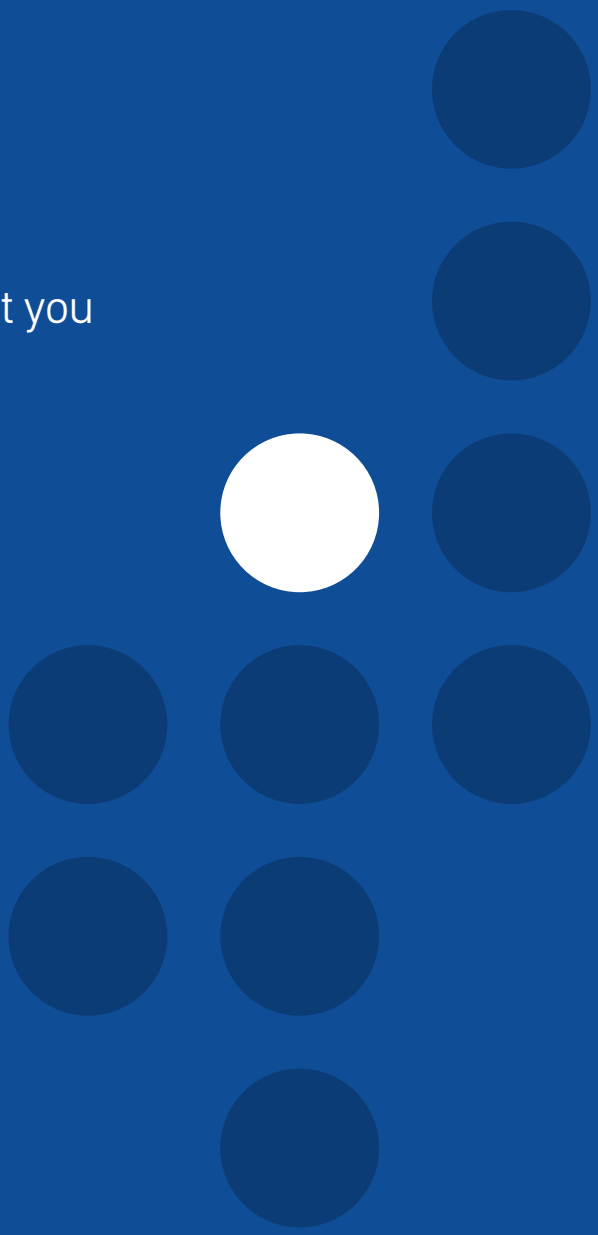
In vivo miRCURY LNA™ microRNA Inhibitors

- Highly potent microRNA inhibition at low dosage in a broad range of tissues
- Superior serum stability and nuclease resistance
- Numerous high impact publications demonstrate therapeutic potential of microRNA

In vivo RNA Silencing using Antisense LNA™ GapmeRs and miRCURY LNA™ microRNA Inhibitors

RNA Target	Tissue	Organism	Process/Disease	Reference
SAMMSON lncRNA	Tumor	Mouse	Melanoma	Leucci *et al.*, 2016, Nature
Chast lncRNA	Heart	Mouse	Cardiac hypertrophy	Viereck *et al.*, 2016, Science Translational Medicine
MALAT1 lncRNA	Endothelial cells (blood vessels)	Mouse	Angiogenesis	Michalik *et al.*, 2014, Circ. Res.
BCAR4 lncRNA	Lung metastatic nodules	Mouse	Breast cancer metastasis	Xing *et al.*, 2014, Cell
miR-221	Various	Mouse (plus toxicology studies in non-human primates)	Multiple Myeloma	Gallo Cantafio *et al.*, Mol. Ther. Nucl. Acids, 2016
miR-802	Liver	Mouse	Diabetes	Kornfeld *et al.*, Nature 2013
miR-33	Liver	Mouse	Cholesterol regulation	Najafi-Shoushtari *et al.*, Science 2010
miR-142-3p	T-cells	Mouse	Graft-versus-host disease	Sun *et al.*, JCI 2015
miR-192	Kidney	Mouse	Diabetic Nephropathy	Putta *et al.*, J Am Soc Nephrol 2012
miR-134	Brain	Mouse	Epilespy	Jimenez-Mateos *et al.*, 2012, Nature Medicine
miR-212	Brain	Rat	Addiction	Hollander *et al.*, Nature 2010
miR-21	Lung	Mouse	Fibrosis	Liu *et al.*, J Exp Med 2010
miR-34a	Heart	Mouse	Cardiac decline/ myocardial infarction	Boon *et al.*, Nature 2013
miR-21-5p	Heart	Mouse	Obesity	Seeger *et al.*, Obesity 2014
miR-199a, miR-1908	Melanoma	Mouse	Melanoma metastasis	Pencheva *et al.*, Cell 2012
miR-712	Aorta endothelium	Mouse	Athersclerosis	Son *et al.*, Nature Commun 2013
miR-33	Eye	Mouse	Age related macular degeneration	Sene *et al.*, Cell Metabolism 2013
miR-21-5p	Bone marrow – hemapoietic stem cells	Mouse	Myelodysplastic	Bhagat *et al.*, Blood 2013
miR-29	Liver, including skeletal muscle	Mouse	Cholesterol and fatty acid synthesis	Kurtz *et al.* Sci Rep 2015

Contact us to discuss how we can assist you
exiqon.com/contact



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