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Investor presentation

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February 2009

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Safe harbor

This presentation contains forward looking statements. The words “believe”, “expect”, “anticipate”, “intend”, “will”, “may”, “would”, “could” and “plan” and similar expressions identify forward looking statements. All statements other than statements of historical facts included in this presentation, including, without limitation, those regarding our financial position, business strategy, plans and objectives of management for future operations (including development plans and objectives relating to our products), are forward looking statements. Such forward looking statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance, achievements to be materially different from any future results, performance, or achievements expressed or implied by such forward looking statements. Such forward looking statements are based on numerous assumptions regarding our present and future business strategies and the environment in which we will operate in the future. The important factors that could cause our actual results, performance or achievements to differ materially from those in the forward looking statements include, among others, risks associated with product development and commercialization, the unenforceability or lack of protection of our patents and proprietary rights, uncertainties related to product manufacturing and supply chain, the lack of market acceptance of our products, our ability to manage growth, the competitive environment in relation to our business area and markets, our ability to attract and retain suitably qualified personnel, our relationships with third parties, changes and developments in technology and third party’s intellectual property rights which our products may become dependant upon, and other factors. Further, certain forward looking statements are based upon assumptions of future events which may not prove to be accurate. The forward looking statements in this document speak only as at the date of this presentation.

- Exiqon at a glance
- Technology & biomarker platforms
- Diagnostics
- Pharma Services
- Life Sciences
- Leveraging our potential
- Financials
- Appendices

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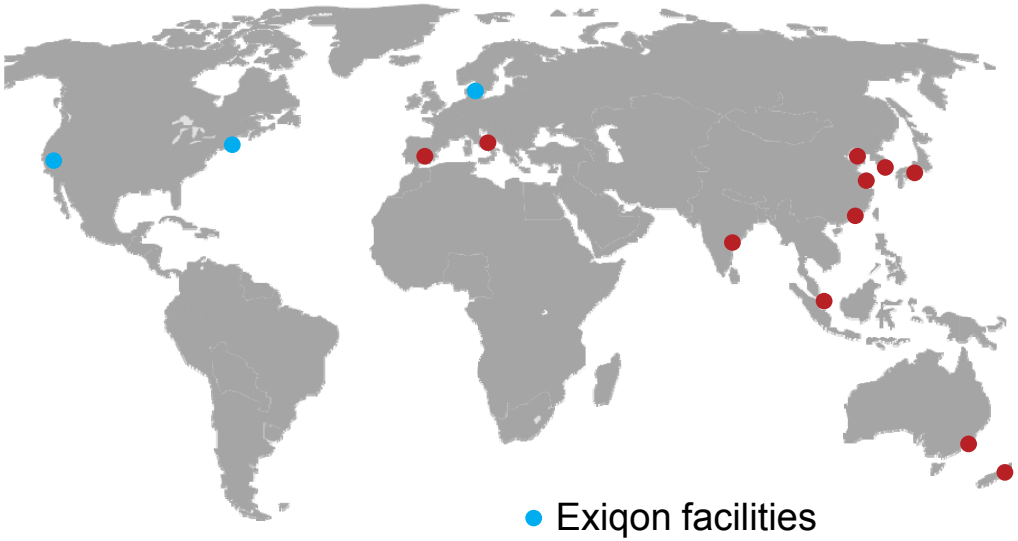
Exiqon at a glance

- Exiqon is dedicated to personalizing cancer treatment selection
- Focus on miRNA biomarkers
- Proprietary LNA™ technology enables unique products
- 174 patents and patent applications cover products and biomarkers (91 issued)
- Established as a market leader
- Funded until expected profitability in 2011
- Listed on NASDAQ OMX, Copenhagen (EXQ)



EXIQON Diagnostics | EXIQON Pharma Services | EXIQON Life Sciences

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Our business is based on superior LNA™ detection technology platform

EXIQON Diagnostics

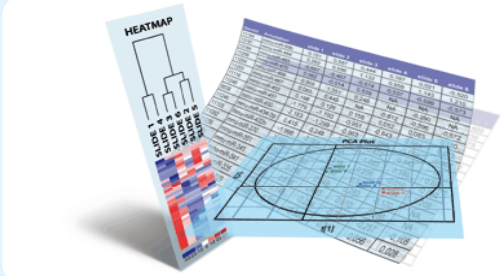
Personalized medicine

Treatment selection strategy:
- Drug resistance
- Prognostics
- Drug metabolism

EXIQON Pharma Services

Services to pharma

Companion diagnostic strategy:
- Biomarker analysis
- Biobank (>150,000)
- Drug resistance



EXIQON Life Sciences

Research products

One-stop supplier strategy:
- miRNA
- Gene expression
- Functional analysis

We address large and fast growing markets

	Market size (mUSD)	Market growth	Exiqon revenue growth 2007-2008	Market drivers
EXIQON Life Sciences	2.000 + (nucleic acid analysis)	10-15%	>140%	Translational research Need for biomarkers
EXIQON Pharma Services	1.000 +	5-10%	100%	Need for biomarkers Access to state of the art knowhow & technology
EXIQON Diagnostics	2.800 +	15-20%	Just entered market	Personalized medicine Functional understanding

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The LNA™ (Locked Nucleic Acid) technology addresses key challenges

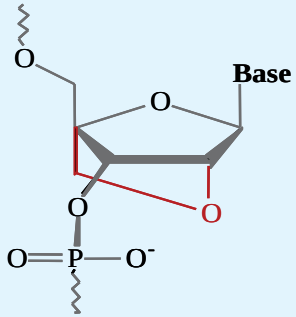
The challenges in nucleic acid detection:

- Lack of specificity
- Lack of sensitivity
- Probes are too long

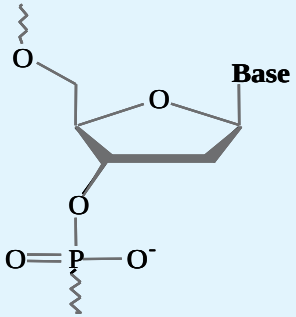
Exiqons LNA™ technology addresses this:

- The chemical properties of LNA™ facilitate much higher specificity
- The chemical properties of LNA™ facilitate stronger binding = increased sensitivity
- The chemical properties of LNA™ facilitate shorter probes

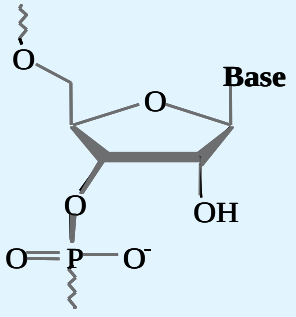
The LNA™ technology improves any kind of DNA and RNA analysis



LNA™



DNA



RNA

Probe \ Target	Perfect match 3'-acgaccac-5'	Single mismatch 3'-acggccac-5'	ΔT_m
DNA 8-mer 5'-tgctggtg-3'	T_m = 35°C	T_m = 25°C	10°C
LNA™ 8-mer 5'-TGCTGGTG-3'	T_m = 71°C	T_m = 45°C	26°C

Perfect for short probes & targets like miRNA

LNA™ (Locked Nucleic Acid): An enabling detection technology

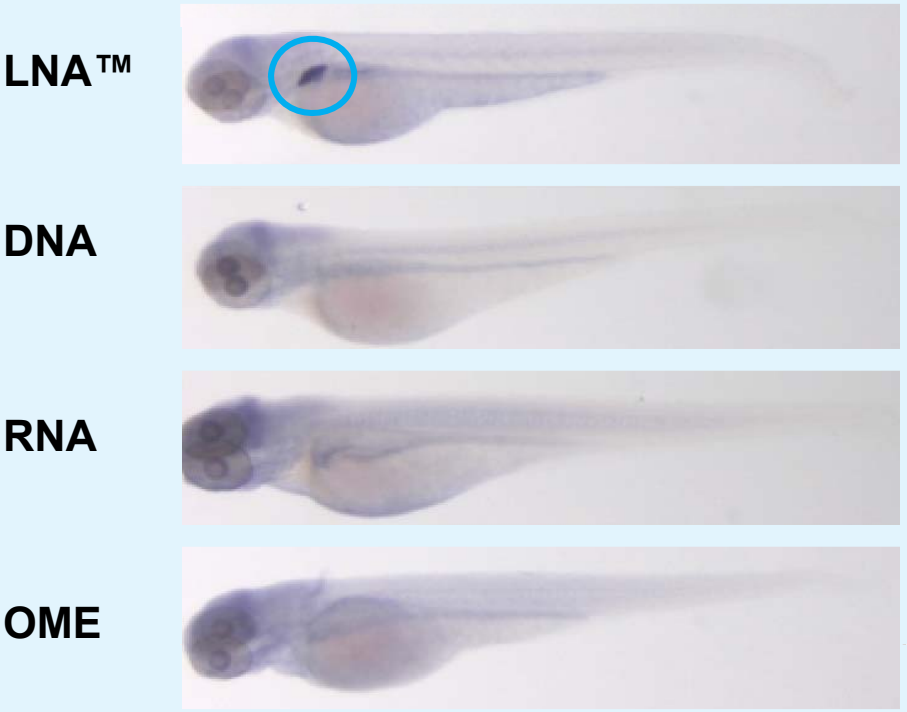
What is LNA™?

- LNA™ is a synthetic RNA molecule

Why is LNA™ unique?

- Provides more specific and sensitive gene expression analysis than any other technology
- Compatible with standard manufacturing and detection equipment

miRNA detection enabled by LNA™



Courtesy of Prof. Ronald Plasterk, Holland

LNA™ enhances any detection platform

Platform	Application	LNA benefits	Exiqon research products	LNA™ in diagnostics
Microarrays	Multiple biomarker	Increased specificity & sensitivity	Yes	Not applied yet
qPCR	High throughput, sensitive	Increased specificity & sensitivity	Yes	Exiqon
Bead-based	High throughput	Increased specificity & sensitivity	Yes	Not applied yet
In situ detection (detection in tissue)	Spatial distribution	Enabling	Yes	Exiqon
Knock down	Functional analysis	Increased biostability	Yes	NA

LNA™ technology: Strong proprietary position (not exhaustive)

Composition of matter (LNA™)		Expire
US 6268490 US 6770748	Composition of LNA™	2018
US 6794499 US 6670461 US 7034133	Composition of LNA™ incl. derivatives	2018
LNA™ applied in products		
US pending	Many LNA™ products	2018
US 11/643615	Many LNA ™products (incl. miRNA)	2023
WO 04/113563	ProbeLibrary™	2024
WO 05/098029	miRNA quantification by qPCR	2025
WO 06/081284	LNA™ in qPCR based on SYBR Green detection	2026
WO 06/069584	miRNA *in situ* detection	2025
207-0065840	miRNA knockdown	2026
2008-0220423 & unpublished	Pre-miR detection	2027
WO-08/040355	PCR primer composition	2027
Unpublished	miRNA labelling	2027
WO 08/074328	miRNA target site blocking	2027
Unpublished	miRNA drug resistance profiles	2028

LNA™ and miRNA biomarkers

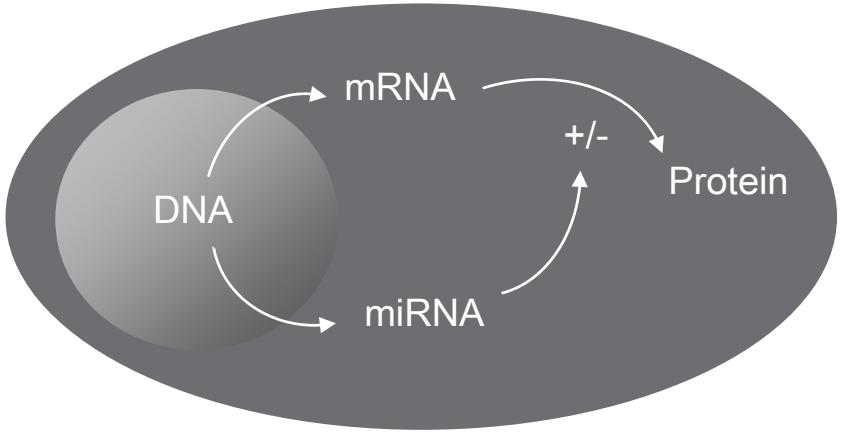
The LNA™ (Locked Nucleic Acid) technology enables Exiqon to make products for analysis of gene expression with higher specificity and increased sensitivity than competing products = *most specific analyses of mRNA and miRNA*

Research business:

Research products for mRNA and miRNA analysis are being applied in drug discovery, target validation, biomarker identification and basic research

Diagnostic business:

Diagnostic products to be based on analysis of miRNA as biomarker. "*Biomarkers are crucial for individualizing, or personalizing, medical treatment…can be used to create more precise classifications of disease to target or stratify therapy*." (FDA's "Critical Path Opportunities Report and List - March 2006)



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Expanding the landscape of biomarkers

miRNAs are:

- Small RNA molecules (19-22nt). Not encoding proteins
- Post-transcriptionally regulating translation of mRNA
- miRNAs are a new group of molecules just recently described

It has been documented that:

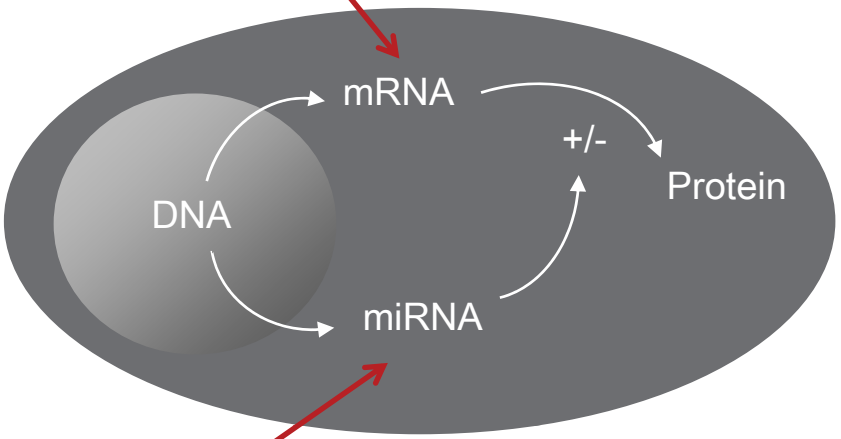
- Altered miRNA expression profiles are associated with the development of a number of diseases. miRNAs are even stable in serum and plasma

miRNAs may be used:

- As diagnostic biomarker
- For disease management
- For prognosis
- For treatment selection
- For stratification of clinical trials
- In companion diagnostics products

miRNA and mRNA: Different biological roles

Universal ProbeLibrary™ product series (Roche/Exiqon products)



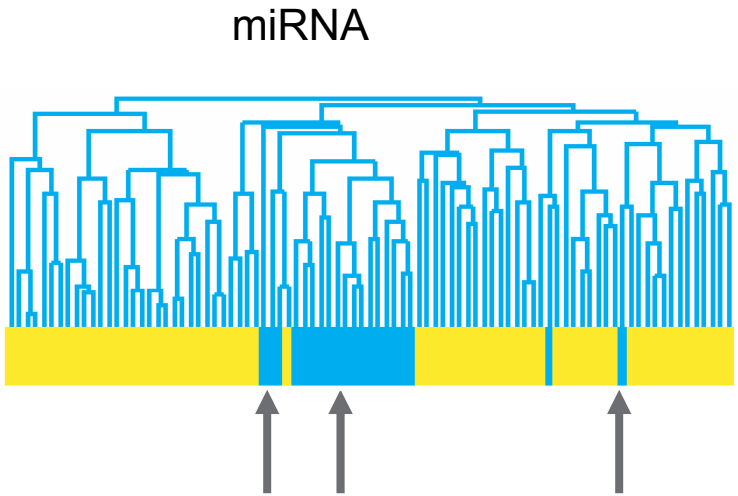
The identity of proteins is determined by mRNA

The amount of proteins is determined by miRNA

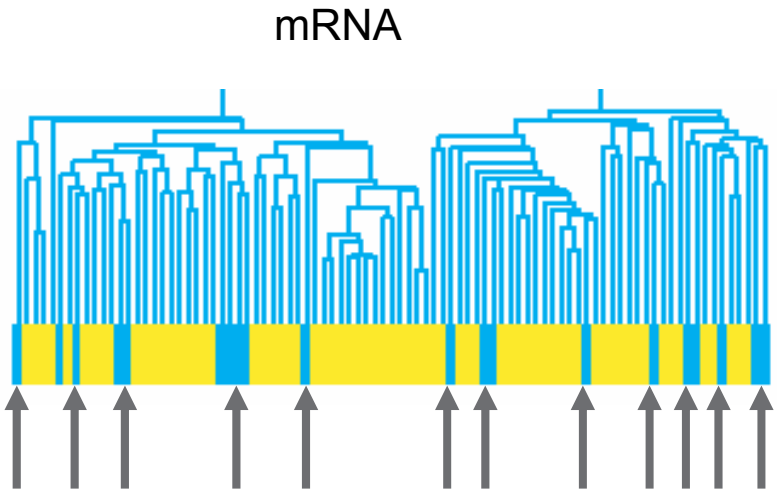
miRCURY LNA ™ (Exiqon products)

miRNA clusters tissues better than mRNA

GI tissue
Non-GI



miRNA profiles cluster the GI samples well
(GI: gastrointestinal origin)



mRNAs do not cluster the GI-samples very well

Conclusion: miRNA expression is more tissue specific than mRNA

Source: Lu *et al*., Nature 2005, v 439; p 834

miRNA and LNA™ provide outstanding opportunities

miRNA is the ideal biomarker:

- miRNA activity is related to cancer – and other diseases
- miRNA is biological stable – even in blood
- miRNA expression with high dynamic range
- Exiqon holds a unique patent position: 4-party co-exclusive license to key patents from Max Planck and The Rockefeller University and hundreds of proprietary miRNA molecules identified by 454 sequencing as well as applications

LNA™ is perfect for detection of miRNA:

- LNA™ is able to monitor even small molecules like miRNA
- LNA ™ is the only technology allowing detection of miRNA directly in tissue
- LNA ™ discriminates even between highly homologous miRNA's – often needed
- Exiqon holds a unique patent position

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miRNA biomarkers: Exiqon's IP in summary (list not exhaustive)

Patent	Application described	Expiration
WO 03/029459	miRNA sequences & applications (Tüschl III)	2022
WO 06/119266 etc.	miRNA sequences & applications (Tüschl III)	2025/26
WO 07/073737	miRNA Cancer of unknown primary markers	2026
Unpublished	miRNA breast cancer markers	2027
WO 08/046911	New miRNA sequences	2027
Unpublished	miRNA & drug resistance	2028

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Personalized disease management in sight

- Molecular diagnostics holds promise of new area in treatment selection
- miRNA are well suited as biomarkers to address large unmet medical need for better cancer treatment selection
- Exiqon is uniquely positioned to address this need with existing and new proprietary product offering

Current generation

Cellular based tests:

Drug resistance (EDR)

Second generation

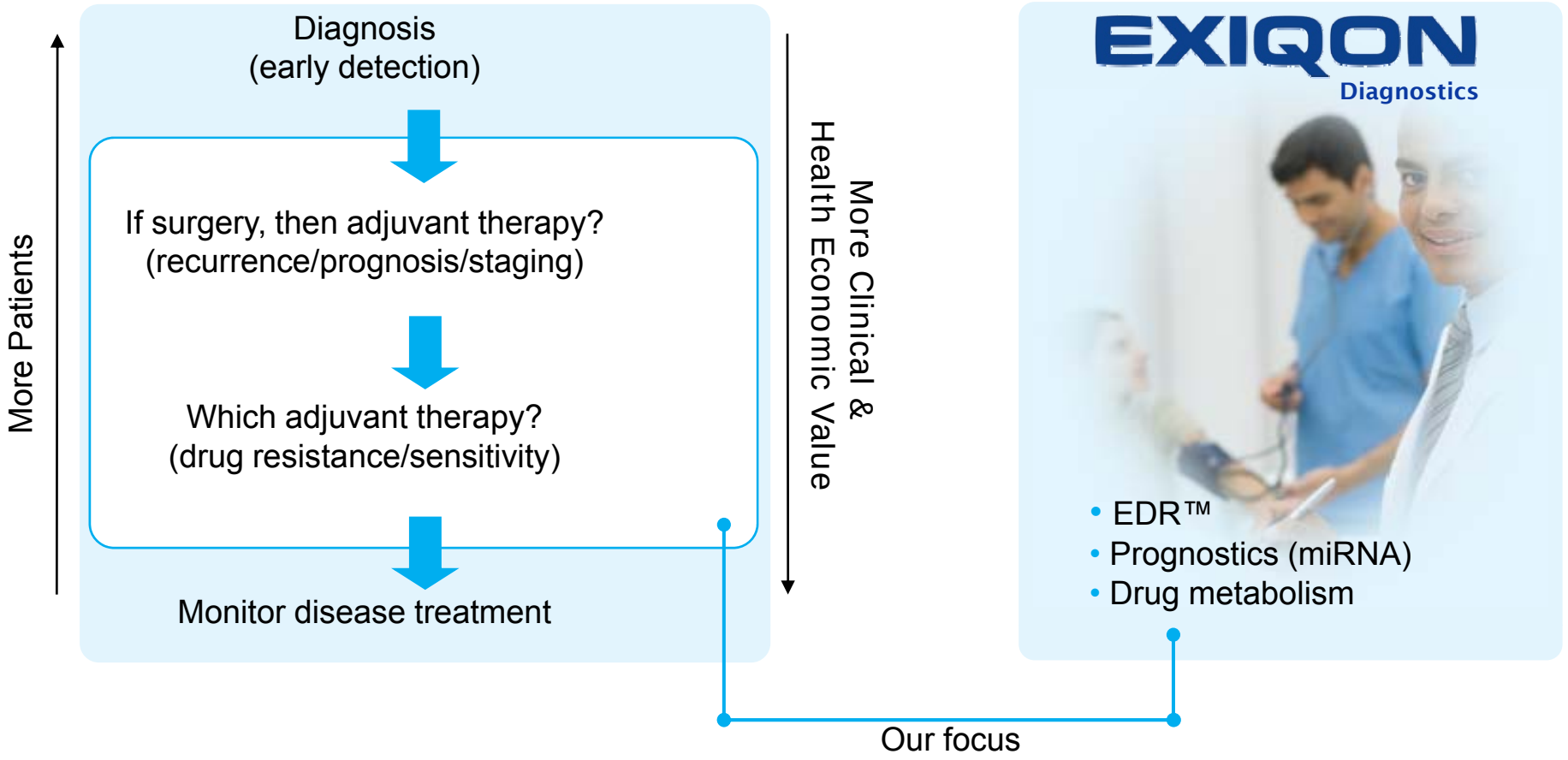
Complimentary molecular and cellular based tests:
Drug resistance testing
Recurrence testing
Predictive testing

Future generations

Molecular based tests:
- Drug resistance
- Recurrence
- Primary origin
- Drug metabolism
- Fully IVD approved kits

Treatment selection → **Disease management**

Exiqon focuses on cancer treatment selection (personalized medicine)



EDR™: Extreme Drug Resistance

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Products and pipeline address a significant unmet market need

Target	Product	Stage	Commercial available	Incidences in the U.S.
Colon (rectal)	EDR™	III & IV	√	42,000
	Recurrence	II	Q1 2009	26,000
Lung	EDR™	II, III & IV	√	143,000
	Recurrence	I	In development	14,000
Ovarian	EDR™	III & IV	√	16,000
Endometrial	EDR™	III & IV	√	10,000
	Recurrence	I & II	In development	28,000
CUP	Tissue identifier		2010	80,000

EDR™: Extreme Drug Resistance

CUP: Cancer of Unknown Primary

Our first miRNA product identifies stage II colon patients likely to recur

	Stage II
Incidence of stage II colon cancer (U.S.)	26,000
Standard of care	Surgery
Recurrence rate	25%
5 year survival after surgery	80%

EXIQON Diagnostics

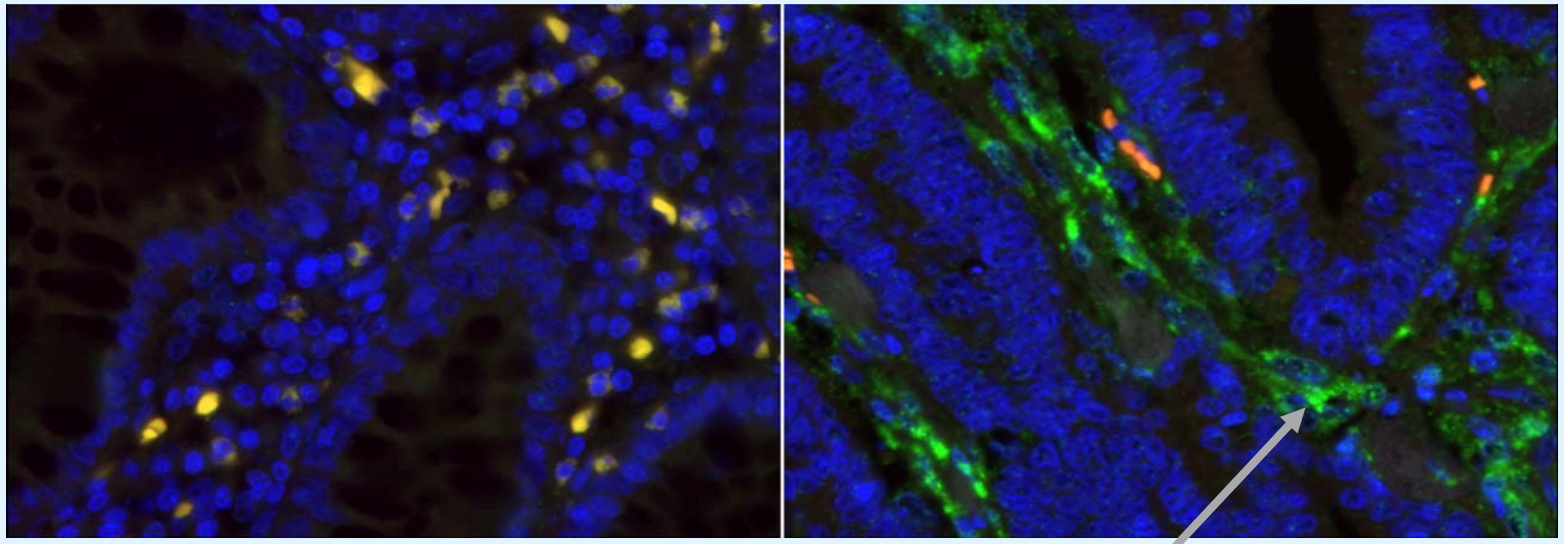
- EDR™
- Prognostics (miRNA)
- Drug metabolism

miRNA-21 appears to be highly expressed in colon tumors

miRNA-21 monitored by *in situ* hybridization enabled by LNA™ probes

Normal colon mucosa

Colon cancer



High miRNA-21 expression (green)

Efficient automated *in situ* hybridization protocol

Automated hybridization platform

Assembled flow-through chamber with slide carrying brain tissue sections after in situ hybridization (ISH). The tissue sections show particular genes (purple precipitation) in specific areas of the mouse brain

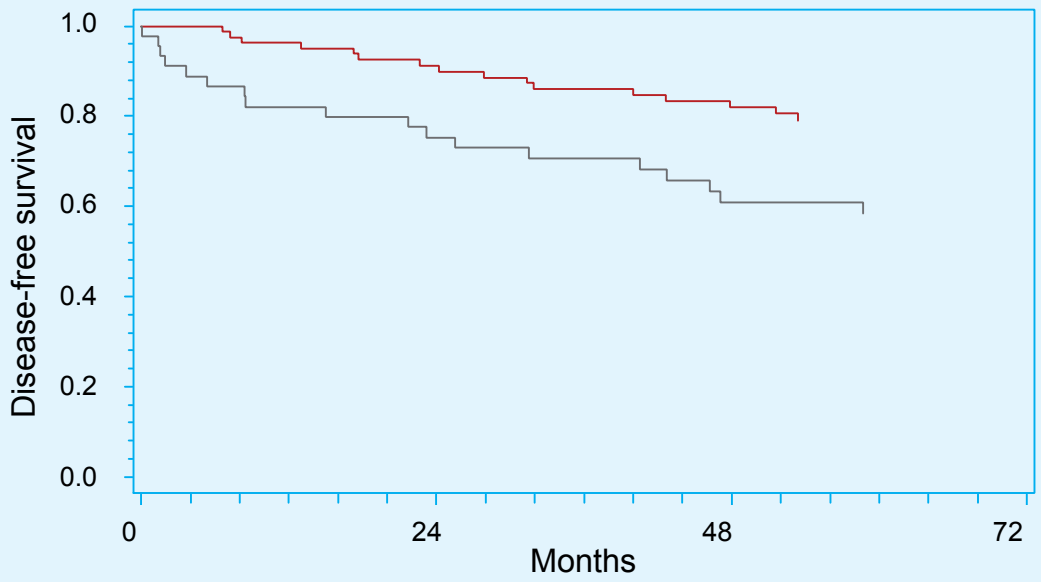
- Tecan Freedom Evo Hybridization system
- Automated 10 hour protocols per 96 patient samples.
- Optimized protocols for FFPE tissue

Automated microscopy platform

- Integrated microscope software analysis system
- Automated 50 slide loader
- Customized software for miRNA analysis – interpretation and data output
- Multiple stations enable rapid test development between sites

High miRNA-21 expression correlates with high risk of recurrence

Analysis of raw data from 130 clinical stage II colon cancer patients



High miRNA-21 expressers
= high risk of recurrence

Low miRNA-21 expressers
= low risk of recurrence

p = 0.009

HR = 2.39 (1.22-4.69)

Looking to the future: miRNA detection in blood (serum and plasma)

It is known that:

- miRNAs are released from solid tumors into the blood stream
- miRNAs are extremely stable in blood (protected by lipid membrane)
- miRNA profile depends on disease state (cancer, diabetes etc.)

Exiqon has build a substantial knowhow in miRNA detection in blood:

- Proprietary LNA™ qPCR platform has been developed for serum/plasma miRNA analysis
- Proprietary miRNA extraction procedures have been developed
- Exiqon holds proprietary miRNA biomarkers
- It has been demonstrated that the serum/plasma miRNA profile depends on tumor state (surgical removal of tumor eliminates tumor specific miRNAs from the serum/plasma)
- May be used for early detection, treatment selection and to monitor disease progression
- Exiqon is actively looking for partnership

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Personalized medicine trend is already picked up by big pharma

"One can say that, except for the very rare instance, Novartis' approach is that [unless] there is a drug with a really solid biomarker attached to it, we don't develop it," Robert Schmouder, executive director of translational medicine at Novartis, said at a Cambridge Healthtech Institute conference on translational medicine, held here last week.

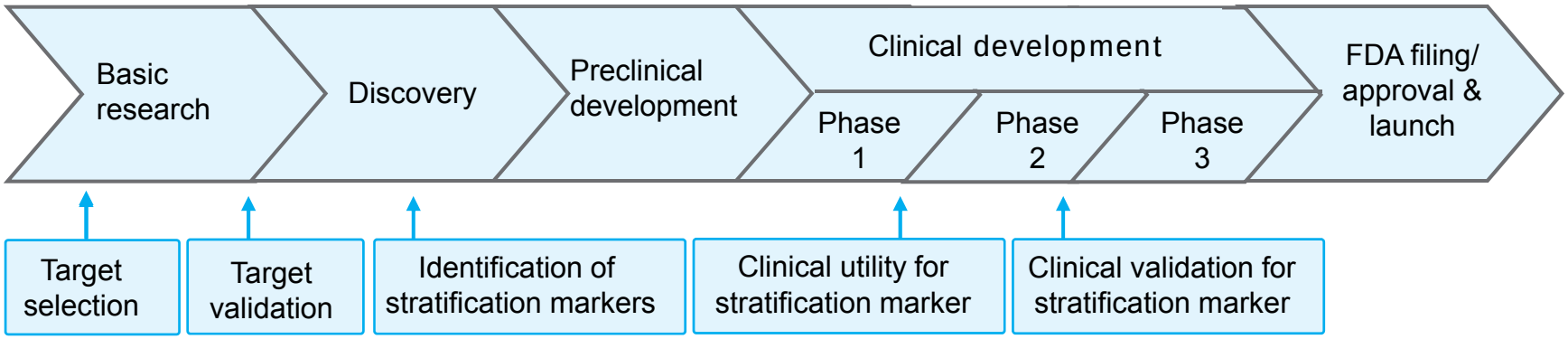
Novartis peers Bristol-Myers Squibb, Wyeth, and Roche, among others, have similarly changed their R&D strategies and pharmacogenomic outlook.

Novartis is not alone in incorporating biomarkers into drug development and embracing the learn-and-confirm model. Encouraged by a willingness at the FDA to accept adaptive clinical trial designs, Novartis is following a larger shift within pharma toward more predictive drug-development strategies.

For instance, Bristol-Myers Squibb uses biomarkers and pharmacogenomics to expand the indications for existing oncologics [see *PGx Reporter 01-10-07*].

Also, Wyeth instated a learn-and-confirm model of its own last year, hoping that in two years the strategy will enable 75 percent of its drug program to have some kind of pharmacogenomic component.

Personalized medicine trend is already picked up by big pharma



- Business unit ”Pharma Services” to accommodate market needs
- Exiqon offers access to miRNA biomarkers and biobank (150,000 tumor samples)
- Exiqon is the only company to offer this including CLIA lab based services

Product offerings in Pharma Services

	Exiqon
Cell Culture	
Primary (drug resistance testing – next generation drugs)	✓
Established	✓
Biobank (tumor bank with extensive databank)	
Primary samples (next generation drug testing, >40.000 samples)	✓
FFPE blocks (>100.000 samples)	✓
Nucleic acid extraction	
Cell Lines (1 & Est)	Planned Q1 2009
FFPE blocks	Planned Q1 2009
Blood	Planned Q1 2009
Analysis (miRNA)	
qPCR	✓
Array	✓
FISH	✓
IHC	✓
ISH	✓

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Exiqon pursues a “one stop supplier” strategy for miRNA research products

Sample preparation	Array profiling	Validation qPCR	Validation *In situ* hybridization	Functional analysis knockdown
				

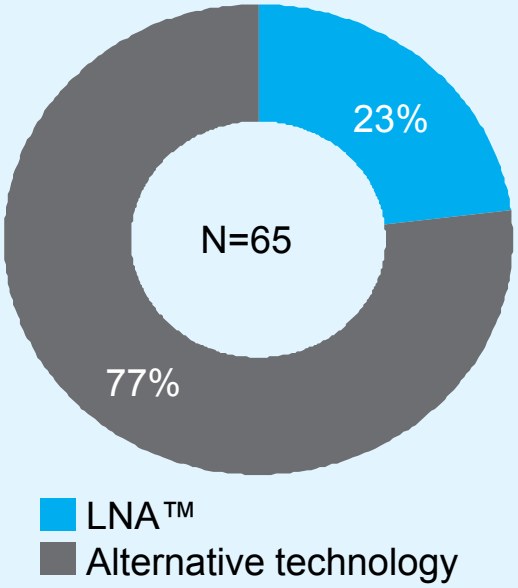
Product offering supports the work-flow for miRNA analysis:

- miRCURY™ sample isolation system, launched Jan 2009
- miRCURY LNA™ microRNA Array System, launched 2006
- miRCURY LNA™ microRNA PCR System, launched Dec 2007 & significantly expanded Sep 2008
- miRCURY LNA™ microRNA Detection Probes, launched 2005
- miRCURY LNA™ microRNA Knockdown System, launched 2006

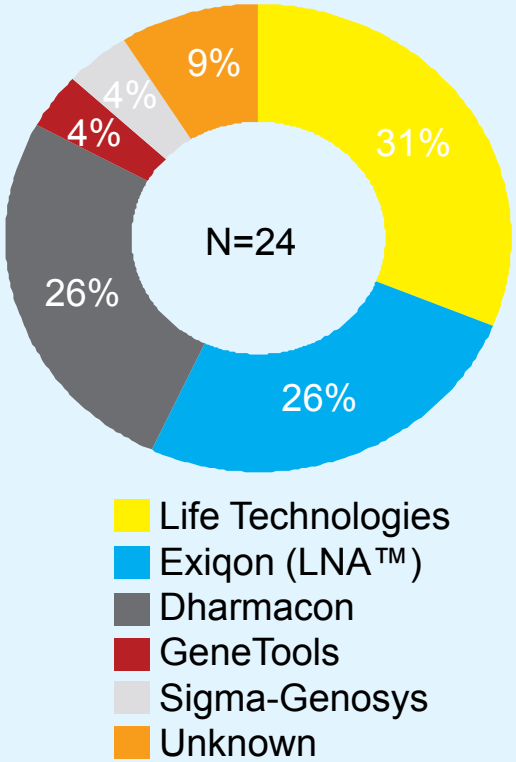
Exiqon is an established leader in the market for miRNA research products

Based on 65 peer reviewed scientific papers published in October 2008:

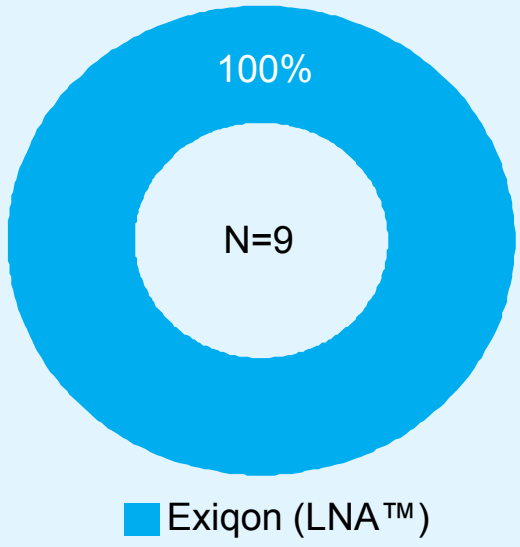
LNA™ applied in miRNA papers



Technology applied in miRNA knock down



Technology applied in miRNA *in situ*



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Broad applications of LNA™ & miRNA (list not exhaustive)

miRNA & LNA™ applications	Technology	Company
Cancer treatment selection	*In situ* hybridization (enabled miRNA detection) & qPCR	Exiqon
Early detection of cancer	qPCR and more (miRNA published biomarkers)	Not pursued yet
Disease monitored in blood	qPCR & arrays (miRNAs are released into the blood stream and are stable)	Exiqon (looking for partner)
Other disease diagnostics	miRNA in metabolic and neural disorders etc. Published	Not pursued yet
Cancer of unknown origin	qPCR of miRNAs	Exiqon
Next next gene sequencing	LNA™ in primers (enabled by LNA™)	Undisclosed
Sample preparation (enrichment for sequencing)	LNA™ in capture probes (enabled by LNA™)	Life Technologies
qPCR of mRNA	LNA™ in Taqman probes (products enabled by LNA™)	Roche
Target validation (siRNA)	LNA ™ in passenger strand (enabled by LNA™)	Life Technologies
Microarrays (SNP, mRNA, CGH, miRNA etc)	LNA enhances any array in terms of sensitivity and specificity	Exiqon (miRNA)
ISH (mRNA, miRNA etc)	LNA™ allows for multiple DIG tags enabling extremely sensitive assays	Exiqon
FISH of chromosomal variation	LNA ™enables extreme sensitivity and speed (1 hour hyb)	Not pursued yet
LNA™ in therapeutics	Antisense & anti-miRs	Santaris & partners

LNA™ opportunities outside our focus are leveraged through partnerships

Roche

Universal ProbeLibrary™

LNA™ enabled mRNA qPCR assays

life technologies™

Silencer®

LNA™ enhanced siRNA

Luminex

FlexmiR™ & FlexSelect™

LNA™ enhanced miRNA detection

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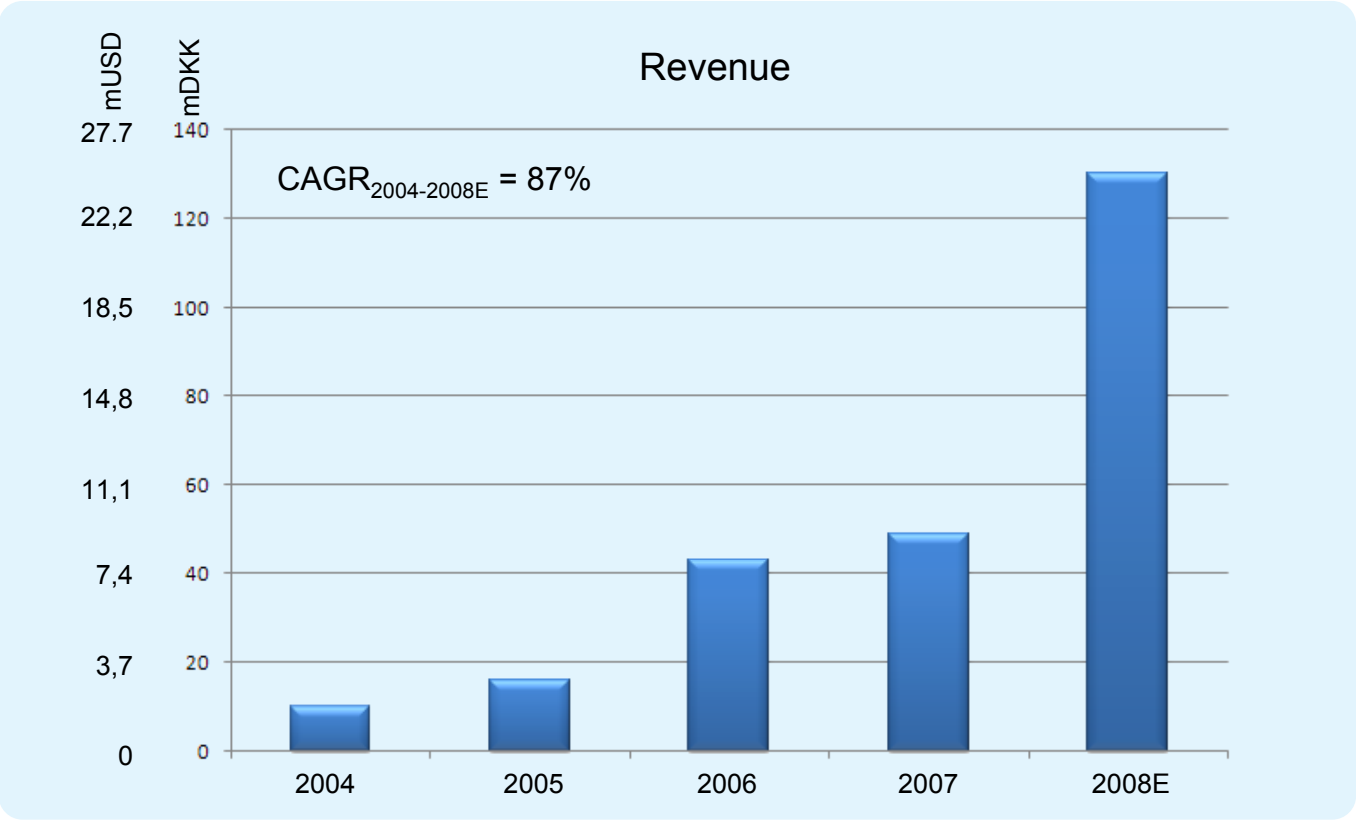
Strong growth



1 USD = 5.4 DKK

- Fully financed until expected profitability in 2011

Key figures – P&L account Q3 2008

DKK '000	Q3 2008	Q3 2007	2007
Product sales	68,554	21,131	38,525
License income	25,387	4,771	6,692
Contract research	1,846	3,635	4,261
Revenue	**95,787**	**29,537**	**49,478**
Production costs	(51,517)	(14,606)	(25,174)
R&D costs	(44,891)	(20,183)	(29,035)
Sales & Marketing costs	(50,786)	(23,785)	(39,080)
Administrative costs	(30,131)	(22,901)	(31,316)
Operating profit (EBIT)	**(81,538)**	**(51,938)**	**(75,127)**
Non-operating income	7,895	4,965	7,341
Profit for the year	**(73,643)**	**(46,973)**	**(67,786)**

Key figures – Balance Sheet Q3 2008

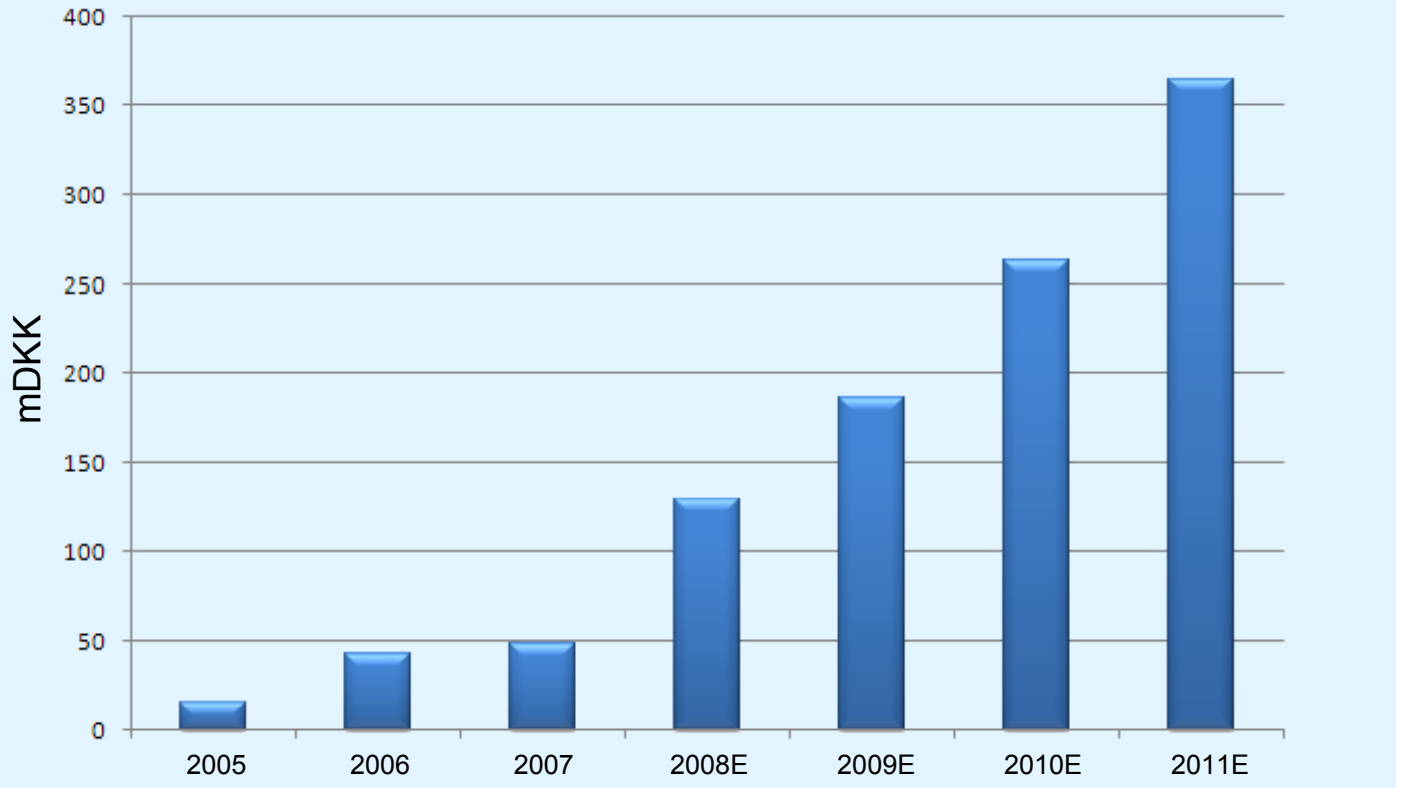
DKK '000	Q3 2008	Q3 2007	2007
Fixed assets	278,116	25,738	36,141
Inventories	15,392	5,058	7,044
Receivables	58,235	10,191	17,266
Cash	189,582	358,397	331,504
Assets	**541,325**	**399,384**	**391,955**
Equity	477,897	361,475	343,366
Long term liabilities	14,774	8,677	7,818
Short term liabilities	48,654	29,232	40,771
Equity & liabilities	**541,325**	**399,384**	**391,955**

Breakdown of Q3 2008 revenue

DKK '000	Q3 2008	Q3 2007	2007
Product sales	68,554	21,131	38,525
License income	25,387	4,771	6,692
Contract research	1,846	3,635	4,261
Total revenue – by type	**95,787**	**29,537**	**49,478**
North America	49,569	17,817	19,417
Europe	44,358	10,547	28,337
Asia	1,860	1,173	1,724
Total revenue – by geography	**95,787**	**29,537**	**49,478**

	Group	Tools	Diagnostics
Revenue – by segment	95,787	67,847	27,940
EBIT	(73,643)	(38,425)	(35,218)

Growth expectations according to analyst report made by Handelsbanken



Source: Handelsbanken Capital Markets, Company updates, April 14, 2008

2009 deliverables & beyond

- Consolidate our leading position in Life Sciences; the market for miRNA analysis
- Expand our miRNA based diagnostic product portfolio
- Pursue new opportunities
  - Identify a partner for the significant opportunity of miRNA in serum
  - Out-license our LNA™ technology to partners operating outside the scope of Exiqon
  - Publish a partnership with a major pharmaceutical partner

Financial goals beyond 2009

- Funded until expected break even by 2011
- Research business expected to be cash positive by end of 2009
- COGS expected to improve over time, particularly during 2008-09
- Margins expected to align with industry standards over time: 65-70%
- R&D costs expected to align with industry standards over time: 15% of revenue
- SG&A costs expected to align with industry standards over time: 30% of revenue

- Exiqon at a glance
- Technology & biomarker platforms
- Diagnostics
- Pharma Services
- Life Sciences
- Leveraging our potential
- Financials
- Appendices

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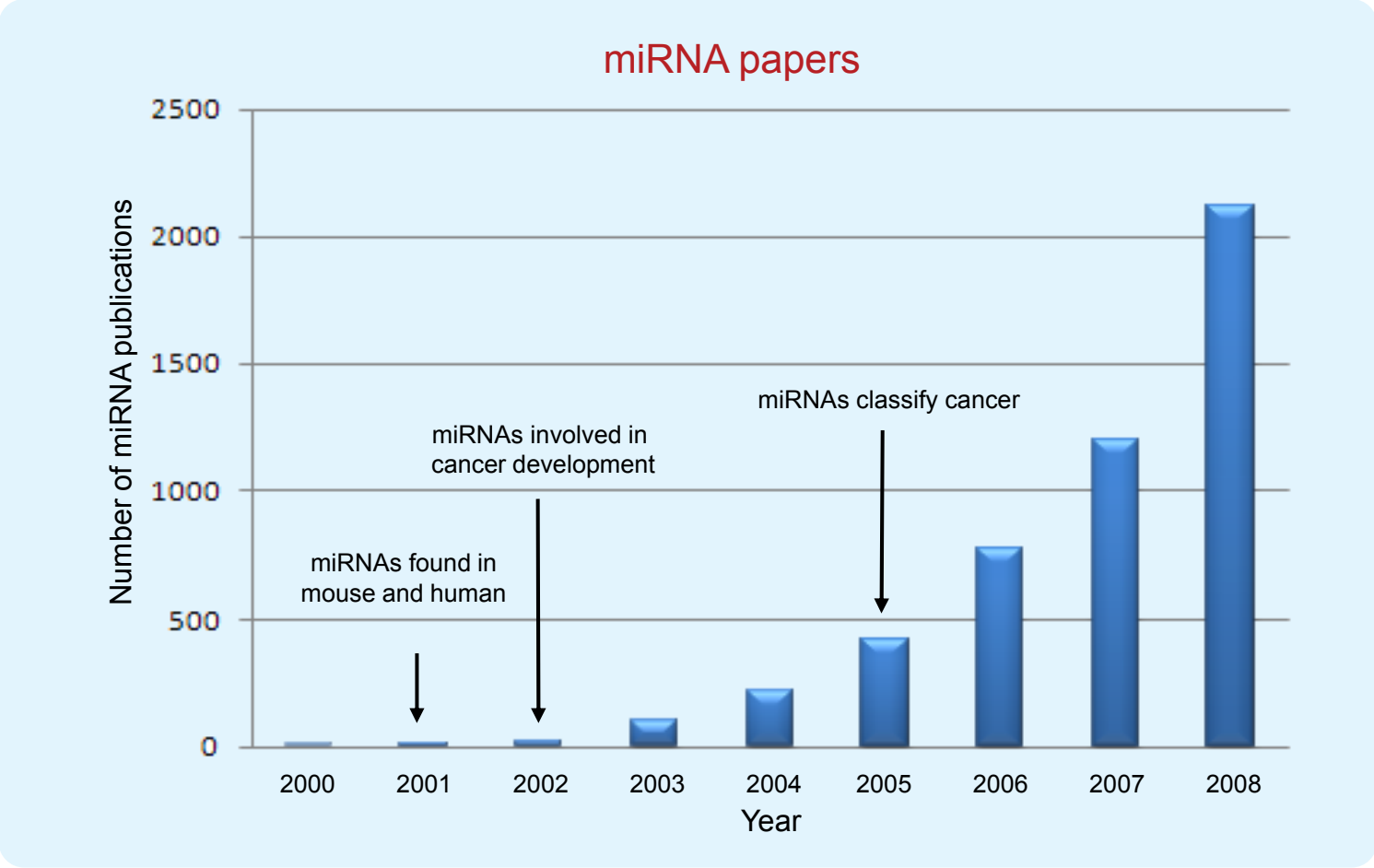
Growing interest in miRNA



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Multiple publications support the use of miRNAs as biomarker in Dx

Research Article

MicroRNA Expression Profiling in Human Ovarian Cancer: *miR-214* Induces Cell Survival and Cisplatin Resistance by Targeting *PTEN*

Hua Yang, William Kong, Lili He, Jian-Jun Zhao, Joshua D. O'Donnell, Jiawang Wang, Robert M. Wenham, Domenico Coppola, Patricia A. Kruk, Santo V. Nicosia, and Jin Q. Cheng

Departments of Interdisciplinary Oncology and Pathology, H. Lee Moffitt Cancer Center and Research Institute and University of South Florida College of Medicine, Tampa, Florida

Abstract

MicroRNAs (miRNA) represent a novel class of genes that function as negative regulators of gene expression. Recently, miRNAs have been implicated in several cancers. However,

miRNAs are dramatically changed in different cell types and different developmental stages, suggesting that miRNA plays a role in cell growth, differentiation, and program

miRNAs are aberrantly expressed or mu

indicating that they may function as a nov

Clinical Chemistry 54:10
1696–1704 (2008)

Cancer Diagnostics

Prognostic Value of Mature MicroRNA-21 and MicroRNA-205 Overexpression in Non–Small Cell Lung Cancer by Quantitative Real-Time RT-PCR

Athina Markou,[1] Emily G. Tsaroucha,[2] Loukas Kaklamanis,[3] Marianthi Fotinou,[2] Vassilis Georgoulias,[4] and Evi S. Lianidou[1]*

MicroRNA Expression Profiles Associated With Prognosis and Therapeutic Outcome in Colon Adenocarcinoma

Aaron J. Schetter, PhD, MPH
Suet Yi Leung, MD
Jane J. Sohn, PhD
Krista A. Zanetti, PhD, MPH
Elise D. Bowman, MS
Nozomu Yanaihara, MD, PhD
Siu Tsan Yuen, MD
Tsun Leung Chan, MD
Dora L. W. Kwong, MD
hD

Context MicroRNAs have potential as diagnostic biomarkers and therapeutic targets in cancer. No study has evaluated the association between microRNA expression patterns and colon cancer prognosis or therapeutic outcome.

Objective To identify microRNA expression patterns associated with colon adenocarcinomas, prognosis, or therapeutic outcome.

Design, Setting, and Patients MicroRNA microarray expression profiling of tumors and paired nontumorous tissues was performed on a US test cohort of 84 patients with incident colon adenocarcinoma, recruited between 1993 and 2002. We evaluated associations with tumor status, TNM staging, survival prognosis, and response to adjuvant chemotherapy. Associations were validated in a second, independent Chinese cohort of 113 patients recruited between 1991 and 2000, using quantitative reverse transcription polymerase chain reaction assays. The final date of follow-up was December 31, 2005, for the Maryland cohort and August 16, 2004, for the Hong Kong cohort.

Main Outcome Measures MicroRNAs that were differentially expressed in tumors and microRNA expression patterns associated with survival using cancer-specific death as the end point.

Results Thirty-seven microRNAs were differentially expressed in tumors from the

Research Article

Diagnostic and Prognostic MicroRNAs in Stage II Colon Cancer

Troels Schepeler,[1] Jørgen T. Reinert,[1] Marie S. Ostenfeld,[1] Lise L. Christensen,[1] Asli N. Silahtaroglu,[2] Lars Dyrskjøt,[1] Carsten Wiuf,[3] Frank J. Sørensen,[3] Mogens Kruhøffer,[1] Søren Laurberg,[4] Sakari Kauppinen,[2,5] Torben F. Ørntoft,[1] and Claus L. Andersen[1]

[1]Molecular Diagnostic Laboratory, Department of Clinical Biochemistry, Aarhus University Hospital, Aarhus N, Denmark; [2]Wilhelm Johannsen Centre for Functional Genome Research, Department of Cellular and Molecular Medicine, University of Copenhagen, Copenhagen N, Denmark; [3]Bioinformatics Research Center, University of Aarhus and [4]Department of Surgery P, Aarhus University Hospital, THG, Aarhus C, Denmark; and [5]Santaris Pharma, Hørsholm, Denmark

MicroRNA Gene Expression Deregulation in Human Breast Cancer

Marilena V. Iorio,[1] Manuela Ferracin,[2] Chang-Gong Liu,[1] Angelo Veronese,[2] Riccardo Spizzo,[2] Silvia Sabbioni,[2] Eros Magri,[2] Massimo Pedriali,[2] Muller Fabbri,[1] Manuela Campiglio,[3] Sylvie Ménard,[3] Juan P. Palazzo,[4] Anne Rosenberg,[5] Piero Musiani,[6] Stefano Volinia,[1] Italo Nenci,[2] George A. Calin,[1] Patrizia Querzoli,[2] Massimo Negrini,[2] and Carlo M. Croce[1]

[1]Comprehensive Cancer Center, Ohio State University, Columbus, Ohio [2]Dipartimento di Medicina Sperimentale e Diagnostica, e Centro Interdipartimentale per la Ricerca sul Cancro, Università di Ferrara, Ferrara, Italy; [3]Molecular Targeting Unit, Department of Experimental Oncology, Istituto Nazionale Tumori, Milan, Italy; Departments of [4]Pathology, Anatomy and Cell Biology and [5]Surgery, Thomas Jefferson University, Philadelphia, Pennsylvania; and [6]C.S.I. Aging Research Center, Chieti, Italy

Abstract

MicroRNAs (miRNAs) are a class of small noncoding RNAs that control gene expression by targeting mRNAs and triggering either translation repression or RNA degradation. Their aberrant expression may be involved in human diseases, including cancer. Indeed, miRNA aberrant expression has been previously found in human chronic lymphocytic leukemias, where miRNA signatures were associated with specific clinicobiological features. Here, we show that, compared with

Among human diseases, it has been shown that miRNAs a aberrantly expressed or mutated in cancer, suggesting that th may play a role as a novel class of oncogenes or tumor suppres genes. The first evidence of involvement of miRNAs in human canc came from molecular studies characterizing the 13q14 deletion human chronic lymphocytic leukemia (CLL), which revealed th two miRNAs, *mir-15a* and *mir-16-1*, were the only genes within t smallest common region of deletion. The same two genes w affected by a chromosomal translocation in a CLL patient. *mir-16* and/or *mir-15a* were then found down-regulated in 50% to 60%

nature Vol 449|11 October 2007|doi:10.1038/nature06174

ARTICLES

Tumour invasion and metastasis initiated by microRNA-10b in breast cancer

Li Ma[1], Julie Teruya-Feldstein[2] & Robert A. Weinberg[1]

MicroRNAs have been implicated in regulating diverse cellular pathways. Although there is emerging evidence that some microRNAs can function as oncogenes or tumour suppressors, the role of microRNAs in mediating cancer metastasis remains unexplored. Here we show, using a combination of mouse and human cells, that microRNA-10b (miR-10b) is highly expressed in metastatic breast cancer cells and positively regulates cell migration and invasion. Overexpression of miR-10b in otherwise non-metastatic breast tumours initiates robust invasion and metastasis of miR-10b is induced by the transcription factor Twist, which binds directly to the putative promoter of *mir-10* (*MIRN10B*). The miR-10b induced by Twist proceeds to inhibit translation of the messenger RNA encoding hom of a well-characterized pro-metastatic gene, *RHOC*. Significantly, the level of cinomas correlates with clinical progression. These findings suggest the work in which a pleiotropic transcription factor induces expression of a specific micro in turn activates another pro-metastatic gene, leading to tumour cell invasion

Frequent deletions and down-regulation of micro-RNA genes *miR15* and *miR16* at 13q14 in chronic lymphocytic leukemia

George Adrian Calin*, Calin Dan Dumitru*, Masayoshi Shimizu*, Roberta Bichi*, Simona Zupo†, Evan Noch*, Hansjuerg Alder*, Sashi Rattan*, Michael Keating‡, Kanti Rai§, Laura Rassenti¶, Thomas Kipps¶, Massimo Negrini*, Florencia Bullrich*, and Carlo M. Croce*‖

*Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA 19107; †Clinical Immunology, National Institute for Research on Cancer, 16132 Genoa, Italy; ‡Department of Leukemia, University of Texas M. D. Anderson Cancer Center, Houston, TX 77030; §Long Island Jewish Medical Center, New Hyde Park, NY 11040; and ¶Department of Medicine, University of California at San Diego, La Jolla, CA 92093

Contributed by Carlo M. Croce, October 7, 2002

Micro-RNAs (*miR* genes) are a large family of highly conserved noncoding genes thought to be involved in temporal and tissue-specific gene regulation. MiRs are transcribed as short hairpin precursors (≈70 nt) and are processed into active 21- to 22-nt RNAs

Research Consortium institutions. Briefly, peripheral blood was obtained from CLL patients, and mononuclear cells were isolated through Ficoll/Hypaque gradient centrifugation (Amersham Pharmacia Biotech) and then processed for RNA and

ARTICLE

PNAS

Tumor-suppressive *miR-34a* induces senescence-like growth arrest through modulation of the E2F pathway in human colon cancer cells

Hiroshi Tazawa, Naoto Tsuchiya, Masashi Izumiya, and Hitoshi Nakagama*

Biochemistry Division, National Cancer Center Research Institute, 5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan

Communicated by Takashi Sugimura, National Cancer Center, Tokyo, Japan, August 4, 2007 (received for review June 6, 2007)

Accumulating evidence suggests a role for microRNAs in human carcinogenesis as novel types of tumor suppressors or oncogenes. However, their precise biological role remains largely elusive. In the present study, we aimed to identify microRNA species involved in the regulation of cell proliferation. Using quantitative RT-PCR analysis, we demonstrated that *miR-34a* was highly up-regulated in a human colon cancer cell line, HCT 116, treated with a DNA-damaging agent, adriamycin. Transient introduction of *miR-34a* into two human colon cancer cell lines, HCT 116 and RKO, caused

be a component of RNA-induced silencing complex (RISC). We also demonstrated its frequent up-regulation in human colon cancers (13). Furthermore, it was also overexpressed in precancerous lesions induced by chemical carcinogens in rats (13). Although the detailed molecular mechanisms underlying the induction of SND1 in colon epithelial cells are not yet clear, alteration of its expression could be accompanied by the changes in the expression of miRNA species caused by some environmental insults. Therefore, we hypothesize that expression of a

Unique microRNA molecular profiles in lung cancer diagnosis and prognosis

Nozomu Yanaihara,[1] Natasha Caplen,[2] Elise Bowman,[1] Masahiro Seike,[1] Kensuke Kumamoto,[1] Ming Yi,[3] Robert M. Stephens,[3] Aikou Okamoto,[4] Jun Yokota,[5] Tadao Tanaka,[4] George Adrian Calin,[6] Chang-Gong Liu,[6] Carlo M. Croce,[6] and Curtis C. Harris[1,*]

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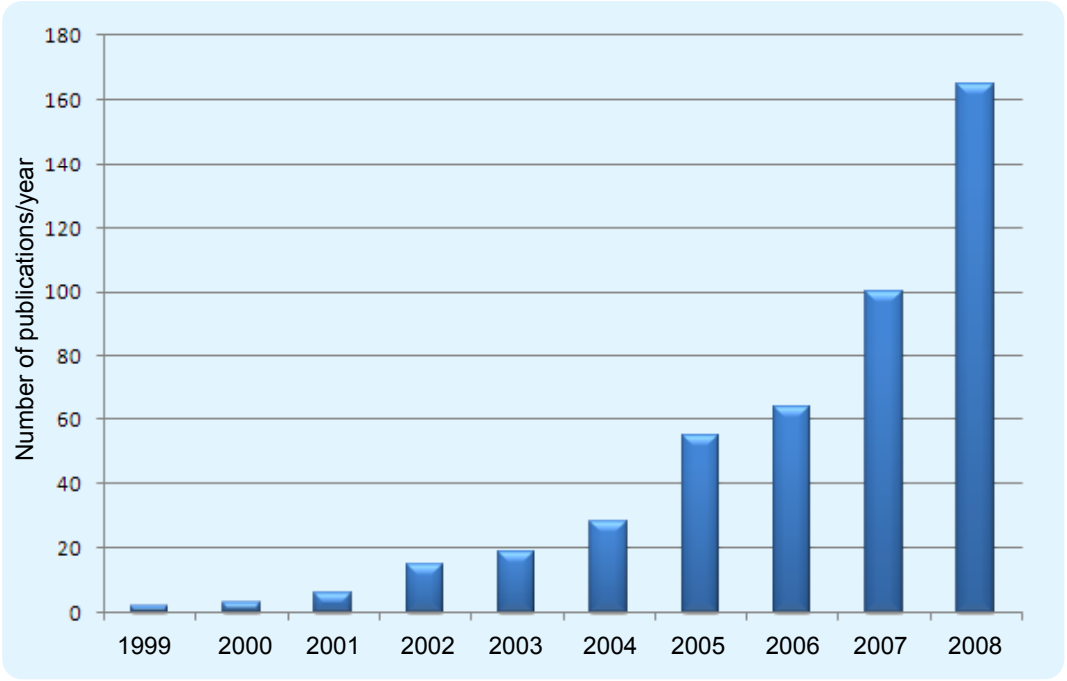
*Correspondence: curtis_harris@nih.gov

LNA™ is well-applied in the Life Science segment

LNA™ is a recognized technology:

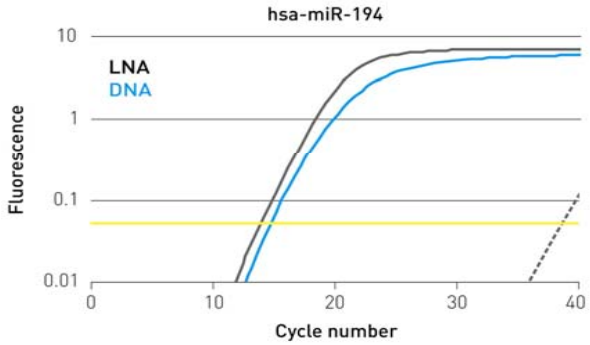
- LNA™ has gone from being a ”spurious” chemistry to an accepted and widely used tool in research
- Over 650 papers citing LNA™ in abstracts alone

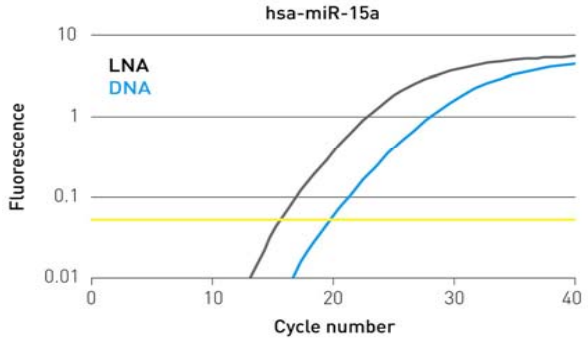
LNA™ paper citations analyzed by HighWire*

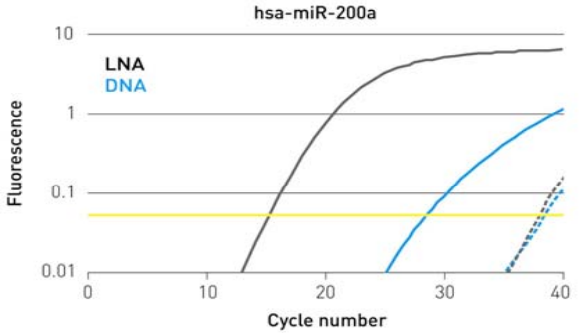


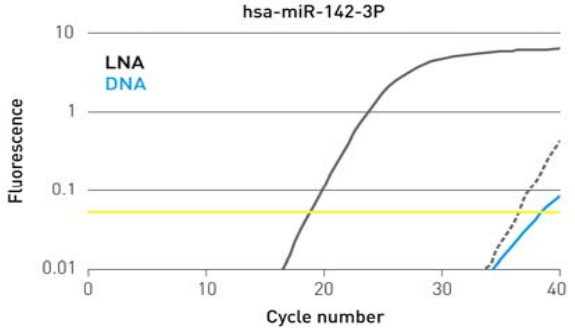
*The actual usage of LNA™ is higher as many papers do not cite LNA ™ anymore and the figure therefore represents the trend

LNA™ improves miRNA qPCR assays and may even rescue some assays









microRNA	%GC	sequence (5′-3′)
miR-194	45	uguaacagcaacuccaugugga
miR-15a	41	uagcagcacauaaugguuugug
miR-200a	41	uaacacugucugguaacgaugu
miR-142-3p	35	uguaguguuuccuacuuuaugga

LNA ™allows for specific amplification of all miRNA targets, even AT rich sequences

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Survey conducted September 2008 (Biotechnique's readers)

3. With which of the following manufacturers are you familiar? (check all that apply)

	Response Percent	Response Count
Agilent	55.8%	92
Applied Biosystems	**85.5%**	141
Combimatrix	8.5%	14
Exiqon	42.4%	70
Genosensor	7.9%	13
Invitrogen	81.8%	135
LC Sciences	11.5%	19
Miltenyi	25.5%	42
Stratagene	64.8%	107
None of these	3.0%	5
answered question		**165**
skipped question		**115**

Survey conducted September 2008

4. Which of the following attributes are most important to you in choosing a research product for your microRNA research? (check up to three)

	Response Percent	Response Count
Compatibility with existing systems	36.3%	58
Competitive pricing	49.4%	79
Ease-of-use	53.1%	85
Performance (sensitivity and specificity)	**90.6%**	145
Pre- and post-sales service/support	11.9%	19
Range of organisms	14.4%	23
Reputation of manufacturer	17.5%	28
Other (please specify)	3.1%	5
answered question		**160**
skipped question		**120**

This is exactly what LNA does

Survey conducted September 2008

5. Which of the following manufacturers would you be most likely to choose?

	Response Percent	Response Count
Agilent	6.8%	11
Applied Biosystems	**34.8%**	56
Combimatrix	0.0%	0
Exiqon	13.0%	21
Genosensor	3.7%	6
Invitrogen	20.5%	33
LC Sciences	3.1%	5
Miltenyi	1.9%	3
Stratagene	3.1%	5
None of these	13.0%	21
answered question		**161**
skipped question		**119**

Exiqon ranks no 2

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Survey conducted September 2008

6. Please motivate your choice of preferred supplier (check all that apply)

	Response Percent	Response Count
It's a well-known supplier of research products in general	44.1%	67
The company is already an established supplier to our institution	34.9%	53
The company has superior products for microRNA research	**55.9%**	**85**
Other (please specify)	7.2%	11
answered question		152
skipped question		128

Survey conducted September 2008

7. We would like your opinion on a microRNA research products offered by Exiqon. Which of the following attributes do you most closely associate with Exiqon's miRCURY LNA™ products (check up to three)

	Response Percent	Response Count
Compatibility with existing systems	16.6%	25
Competitive pricing	13.9%	21
Ease-of-use	18.5%	28
Performance (sensitivity and specificity)	38.4%	58
Pre- and post-sales service/support	7.3%	11
Range of organisms	7.9%	12
Reputation of manufacturer	9.9%	15
Not familiar with this product	**44.4%**	67
Other (please specify)	3.3%	5
	answered question	151
	skipped question	129

Peers in Danish biotech (the past year)

International SmallCap biotech peers (the past year)

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