PANAGENE

주식회사 파나진

Peptide Nucleic Acid (PNA)

PNA is one of the most successful artificial oligonucleotide mimetics

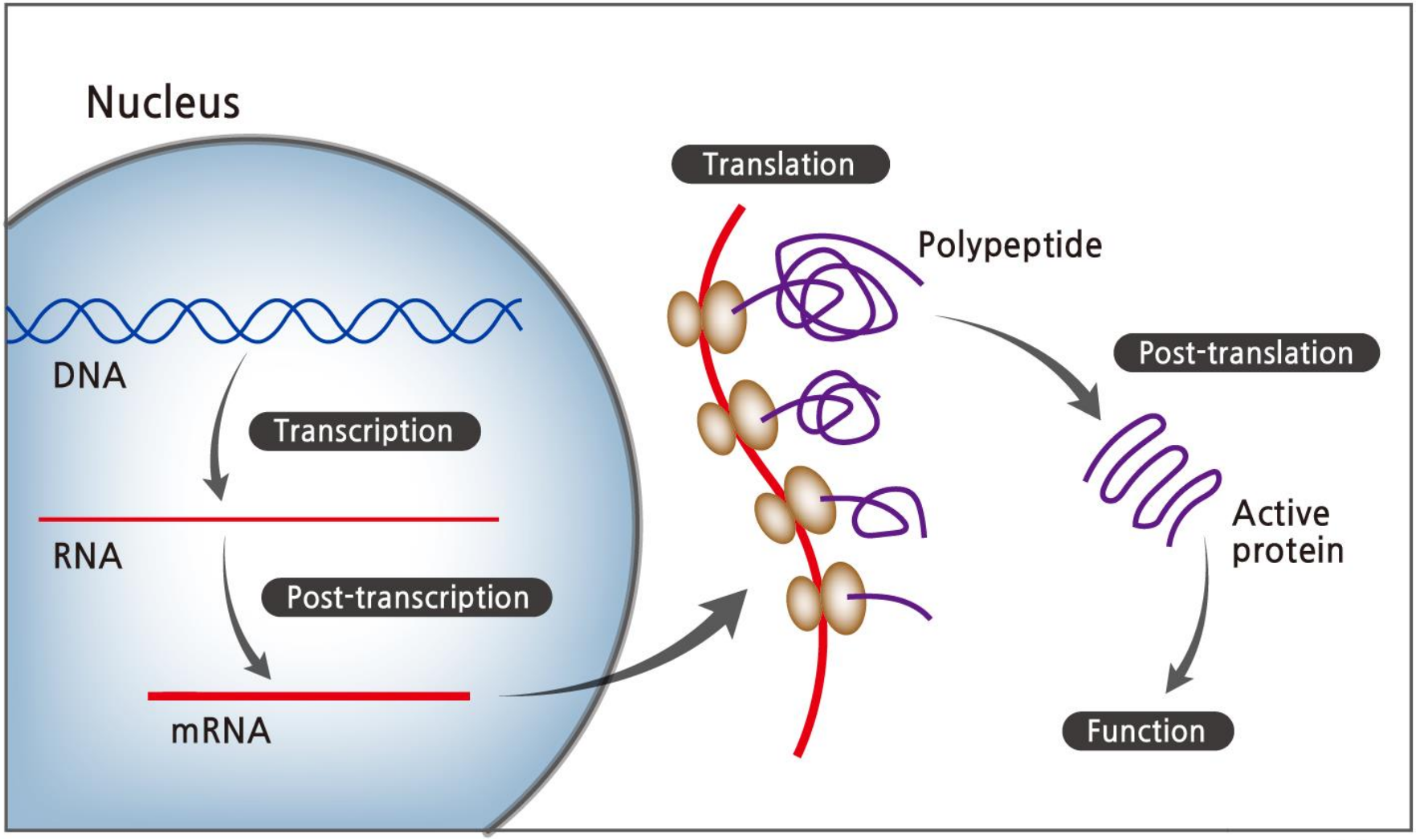
Sung Kee Kim, Ph.D.

CEO of PANAGENE

Table of Contents

1. Overview of PNA
2. Therapeutic Applications
3. Diagnostic Applications
4. What is PANAGENE doing with PNA

Central Dogma



Nucleic Acid Research

Natural

DNA, RNA

Artificial

PNA, LNA, MNA, etc.

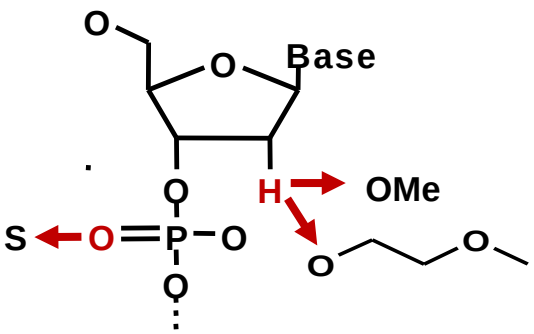
- **Recognition specificity**
- **Metabolic stability**
- **Chemical & physical stability**
- **Chemical modification for biological property**

Applications

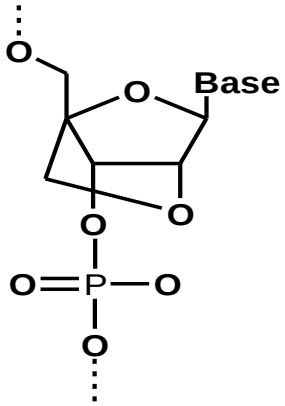
Therapeutics
Molecular Biology
Molecular Diagnostics

Modified Nucleic Acid

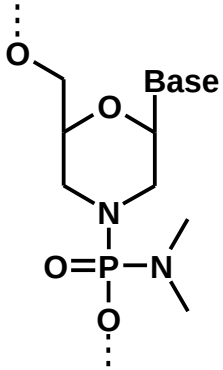
- Affinity & Specificity – Better recognition to DNA or RNA than DNA
- Resistance to enzymes (nuclease, protease)
- Durability to chemical & physical environment
- Cell permeability
- Convenience in synthesis



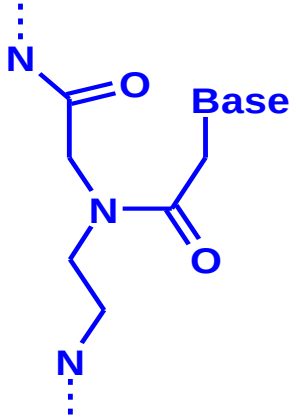
1st and 2nd generation



LNA (Locked NA)

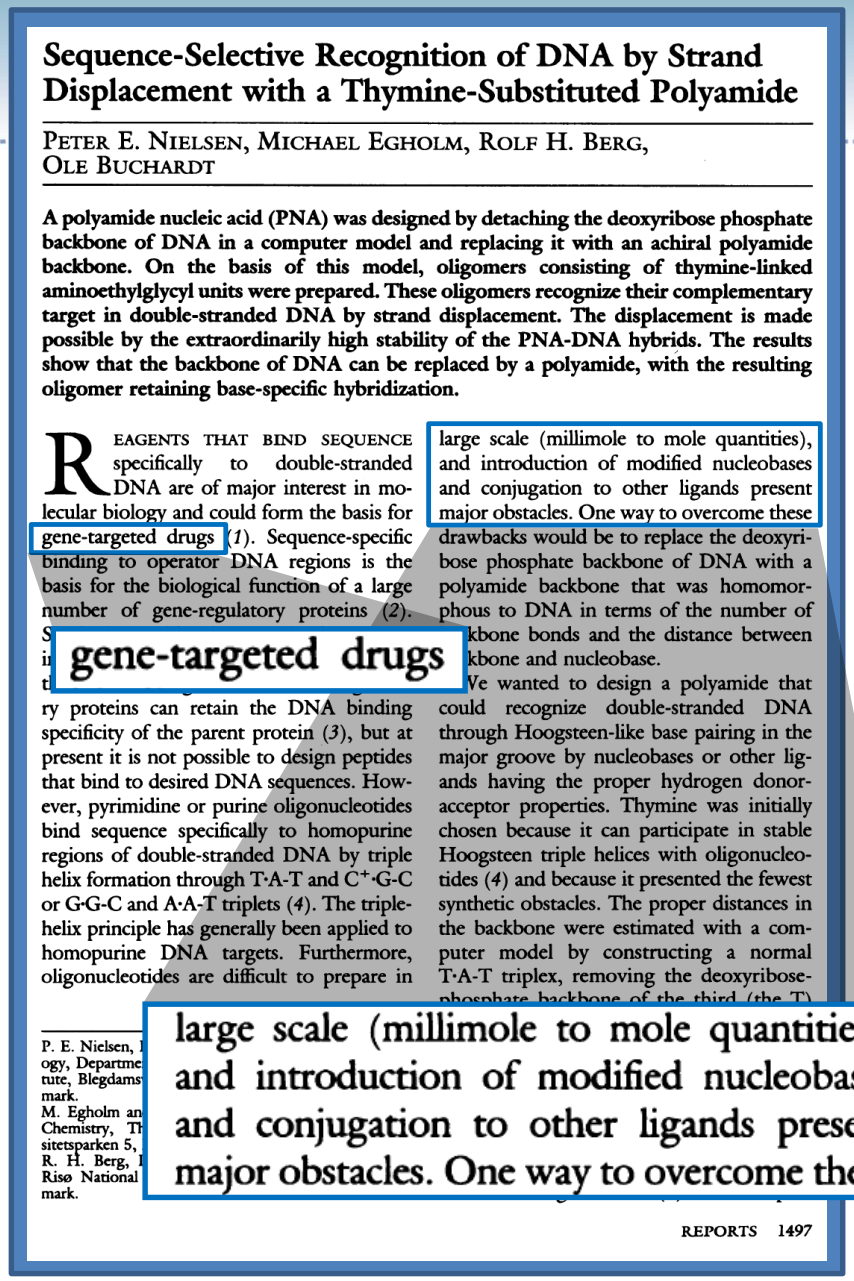


MNA (Morpholino NA)



PNA (Peptide NA)

Overview of PNA



Sequence-Selective Recognition of DNA by Strand Displacement with a Thymine-Substituted Polyamide

PETER E. NIELSEN, MICHAEL EGHOLM, ROLF H. BERG, OLE BUCHARDT

A polyamide nucleic acid (PNA) was designed by detaching the deoxyribose phosphate backbone of DNA in a computer model and replacing it with an achiral polyamide backbone. On the basis of this model, oligomers consisting of thymine-linked aminoethylglycyl units were prepared. These oligomers recognize their complementary target in double-stranded DNA by strand displacement. The displacement is made possible by the extraordinarily high stability of the PNA-DNA hybrids. The results show that the backbone of DNA can be replaced by a polyamide, with the resulting oligomer retaining base-specific hybridization.

REAGENTS THAT BIND SEQUENCE specifically to double-stranded DNA are of major interest in molecular biology and could form the basis for gene-targeted drugs (*1*). Sequence-specific binding to operator DNA regions is the basis for the biological function of a large number of gene-regulatory proteins (*2*). S… i… t… ry proteins can retain the DNA binding specificity of the parent protein (*3*), but at present it is not possible to design peptides that bind to desired DNA sequences. However, pyrimidine or purine oligonucleotides bind sequence specifically to homopurine regions of double-stranded DNA by triple helix formation through T·A-T and C^+·G-C or G·G-C and A·A-T triplets (*4*). The triple-helix principle has generally been applied to homopurine DNA targets. Furthermore, oligonucleotides are difficult to prepare in large scale (millimole to mole quantities), and introduction of modified nucleobases and conjugation to other ligands present major obstacles. One way to overcome these drawbacks would be to replace the deoxyribose phosphate backbone of DNA with a polyamide backbone that was homomorphous to DNA in terms of the number of …kbone bonds and the distance between …kbone and nucleobase. We wanted to design a polyamide that could recognize double-stranded DNA through Hoogsteen-like base pairing in the major groove by nucleobases or other ligands having the proper hydrogen donor-acceptor properties. Thymine was initially chosen because it can participate in stable Hoogsteen triple helices with oligonucleotides (*4*) and because it presented the fewest synthetic obstacles. The proper distances in the backbone were estimated with a computer model by constructing a normal T·A-T triplex, removing the deoxyribose-phosphate backbone of the third (the T)

gene-targeted drugs

large scale (millimole to mole quantities), and introduction of modified nucleobases and conjugation to other ligands present major obstacles. One way to overcome these

P. E. Nielsen, I… ogy, Departme… tute, Blegdams… mark.
M. Egholm an… Chemistry, Th… sitetsparken 5,
R. H. Berg, I… Risø National … mark.

- Described in 1991 by Nielsen, Egholm, Buchardt, Berg.
- ABI (now ThermoFisher) invented Fmoc method in 1995.
- PANAGENE invented Bts method in 2002
- PANAGENE developed the first automatic PNA synthesizer in 2006
- More than 2,500 publications
  - Review (300)
  - Chemistry & properties (2,000)
  - Molecular biology (150)
  - Diagnostics (800)
  - Therapeutics (1,000)
- PANAGENE is a major PNA oligomer supplier
- A variety of diagnostic products are on the market by PANAGENE, etc..

Science (1991) 254:1497

PNA Applications

Therapeutic applications

- Antimicrobial
- Anticancer
- Gene therapy
- Gene editing

Molecular biology & diagnostics applications

- miRNA inhibitor and detection
- PCR clamping
- Microarray
- Mutation detection
- Pathogen detection
- Drug resistance detection
- Companion diagnostics
- Monitoring disease related gene expression

Therapeutic Applications of PNA

Attractive Properties

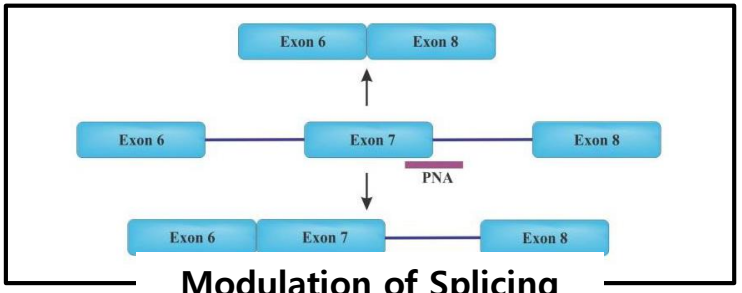
- Resistance to nuclease and protease-mediated degradation
- Very good hybridization affinity to target sequence
- Excellent mismatch sequence discrimination

Limitations

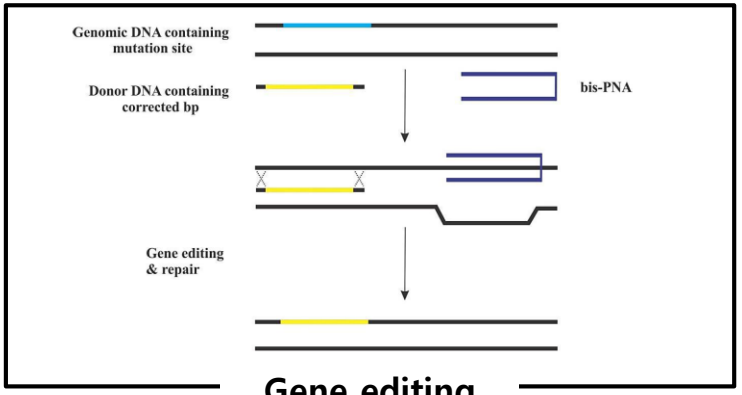
- Poor water solubility
- Poor cellular uptake

Potential categories

- Antigene & Antisense
- Modulation of Splicing
- Gene editing



Modulation of Splicing

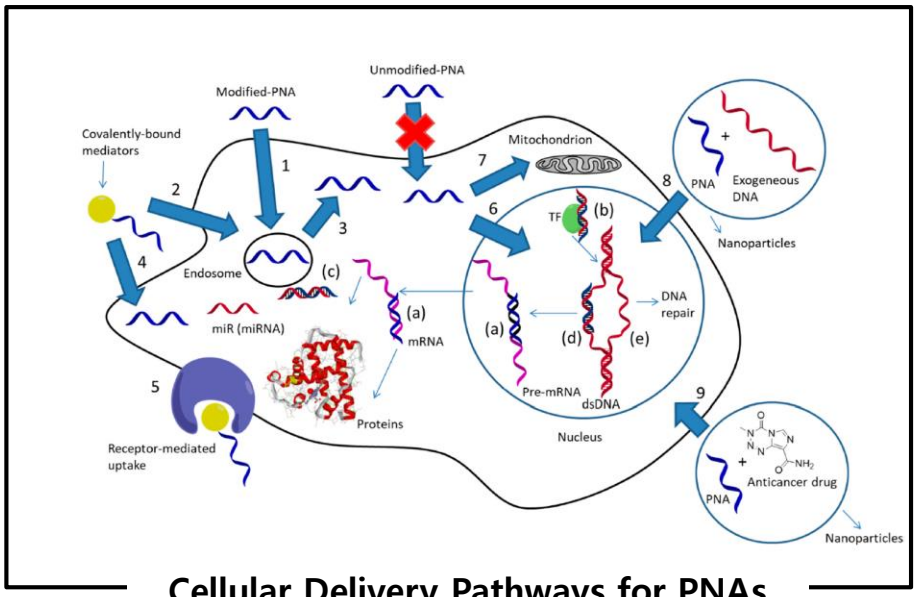


Gene editing

Advanced Pharmaceutical Bulletin (2018) 8(4):551-563

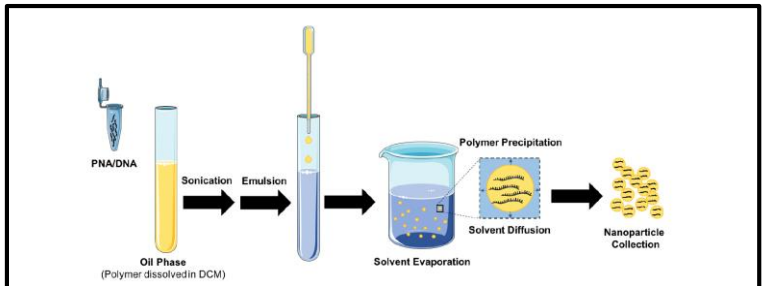
PNA Modifications for Cellular Uptake

1. Formulation of PNA as a duplex with sacrificial DNA
2. Conjugation of PNA oligomers with CPPs or lipophilic moiety (B12, cholesterol, etc.)
3. Backbone or BASE modification of PNA (GPNAs, miniPEGPNA, Olipass, etc.)
4. Formulation negative charged PNA with cationic lipid transfection reagent
5. Incorporation of naked PNA with liposome
6. Loading in biodegradable nanoparticles (PLGA)
7. Loading PNA on graphene oxide.



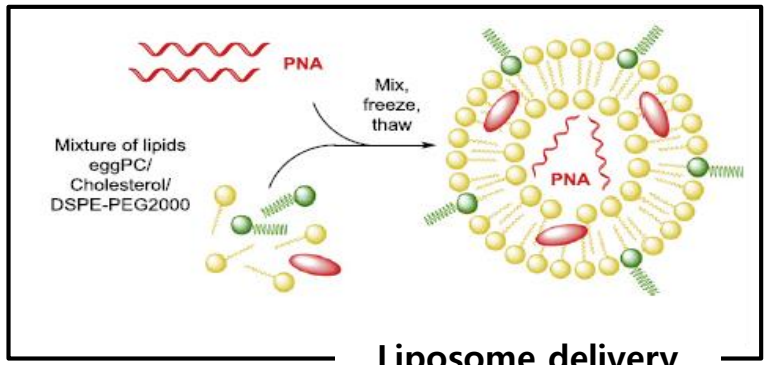
Cellular Delivery Pathways for PNAs

Pharmaceuticals (2021) 14:14



Formulation of PNA/DNA Nanoparticles

Molecules (2018) 23:632



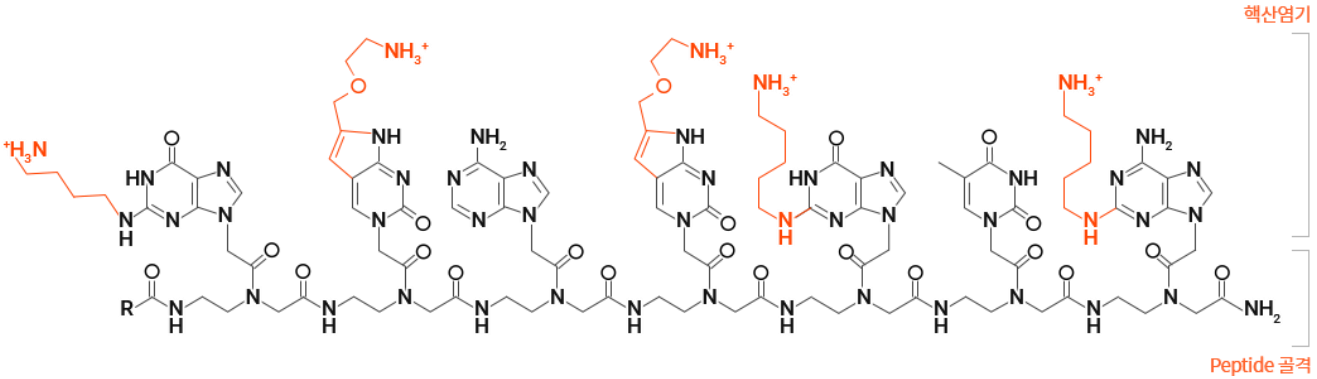
Liposome delivery

Current Opinion in Chemical Biology (2019) 52:112-124

Companies for PNA-based Therapeutics

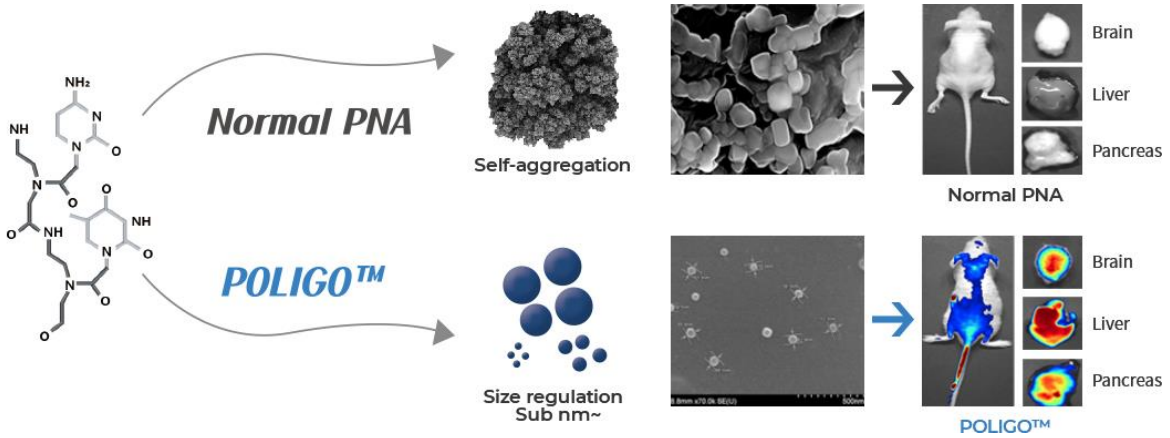
Base modification

source : www.olipass.com



Nanoparticle formation

source: www.seasuntx.com



Several Examples of PNA-mediated Gene Therapy

PNA	Target site	In vivo / in vitro	Disorder	Observed Effects
Antigene PNA	COL1A1 gene	Normal human fibroblast cell line	Fibroproliferative Disorders	Reduction of mRNA level
Antigene PNA	RAD51 gene	Human MM cell line H929 & a SCID-rab mouse model	Multiple Myeloma (MM)	Inhibition of RAD51 expression
Antigene PNA	MYCN gene	Rhabdomyosarcoma cell line	Rhabdomyosarcomas	Reduction of MYCN expression
Antisense PNA	COL7A1 gene	in vitro/ Primary adult fibroblast cultures	Dominant Dystrophic Epidermolysis Bullosa	Inhibition of the transcription of a mutant COL7A1
Antisense PNA	miR-155	Mice	Lymphomas	Inhibition of oncomiR-155
Antisense PNA	miR-221	Human breast cancer MCF-7 & MDA-MB-231 cell lines	Breast Tumors	Inhibition of onco miR-221
Antisense PNA	miR-509-3p	A549 cell lines	Cystic Fibrosis	Inhibition of miR-509-3p
Antisense PNA	Targeting LTR Direct Repeats of HBV RNA	HEPG2 cell line& an acute hepatitis B mouse model	Hepatitis B	Decline in HBV DNA
γPNA and donor DNA	Intron containing Mutation(the IVS2-654)	in vivo (β-globin/eGFP transgenic mouse)	β-thalassaemia	Induce DNA repair in mutaded gene
Antigene	Dystrophin Gene in Muscle Stem Cells	ex vivo/ in mdx mice, a mouse model of DMD	Duchenne muscular dystrophy	Permanently correct single-point mutations at the genomic level in stem cells

Advanced Pharmaceutical Bulletin (2018) 8(4):551-563

PNA as a Potential Anti-infective Agent

- More than 200 publications
- Potential synergistic combination with antibiotics
- Need further research for drug
- Potential against multi-drug bacterial resistance

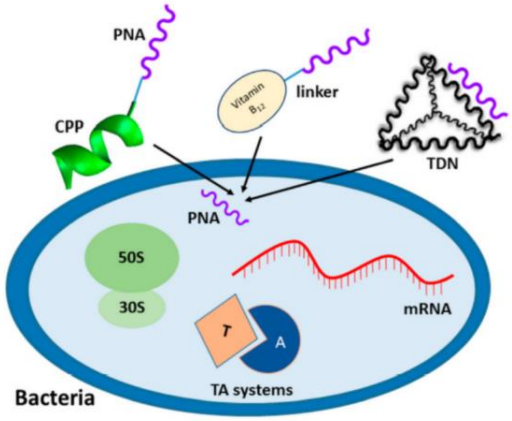


Table 2. Clinical application in bacterial diseases

Target bacteria	Target gene	Function	Bacterial penetrating peptide	Application (*In vitro*/*In vivo*)	References
Escherichia coli	23S rRNA	Bacterial translation and growth	$(KFF)_3K$	*In vitro*	Xue-Wen *et al.* (2007)
ESBLs-*E. coli*	*rpoD*	RNA polymerase sigma factor	$(KFF)_3K$, $(RXR)_4XB$	*In vitro*, *In vivo**	Bai *et al.* (2012)
MDR-*E. coli*	*rpoD*	RNA polymerase sigma factor	$(KFF)_3K$, $(RXR)_4XB$	*In vitro*	Bai *et al.* (2012)
MDR-*Salmonella enterica*	*rpoD*	RNA polymerase sigma factor	$(KFF)_3K$, $(RXR)_4XB$	*In vitro*	Bai *et al.* (2012)
ESBLs-*Klebsiella pneumoniae*	*rpoD*	RNA polymerase sigma factor	$(KFF)_3K$, $(RXR)_4XB$	*In vitro*	Bai *et al.* (2012)
Campylobacter jejuni	*cmeABC*	Multidrug efflux transporter	$(KFF)_3K$	*In vitro*	Jeon and Zhang (2009), Oh *et al.* (2014)
MDR-*Shigella flexneri*	*rpoD*	RNA polymerase sigma factor	$(KFF)_3K$, $(RXR)_4XB$	*In vitro*, *In vivo**	Bai *et al.* (2012)
S. aureus	*fmhB*	Cell wall biosynthesis	$(KFF)_3K$	*In vitro*	Nekhotiaeva *et al.* (2004)
	gyrA	DNA replication	$(KFF)_3K$	*In vitro*	Nekhotiaeva *et al.* (2004)
MRSA	*mecA*	Penicillin-binding protein (PBP2a)	$(KFF)_3K$	*In vitro*	Goh *et al.* (2015)
Streptococcus pyogenes	*gyrA*	DNA gyrase	$(KFF)_3K$	*In vitro*	Patenge *et al.* (2013)
Mycobacterium smegmatis	*inhA*	Mycolic acid biosynthesis	$(KFF)_3K$	*In vitro*	Kulyte *et al.* (2005)

* *In vivo* application of PNA in BALB/c mice.
ESBL, Extended-spectrum beta-lactamases; MDR, Multidrug-resistant; MRSA, Methicillin-resistant *S. aureus*.

Diagnostic Applications of PNA

Attractive Properties

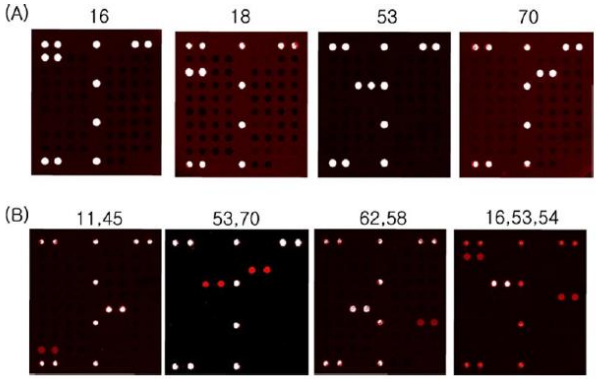
- Physical, chemical and biological stability
- Excellent kinetics in hybridization
- Strong affinity in hybridization
- Excellent mismatch sequence discrimination
- Ease of modification and sequence design

Limitations

- Not applicable as a primer
- Applying PNA requires optimized conditions of PNA and other reagents different from conventional DNA methods

PNA Microarray

PANAGENE developed and commercialized HPV PNA microarray in 2009

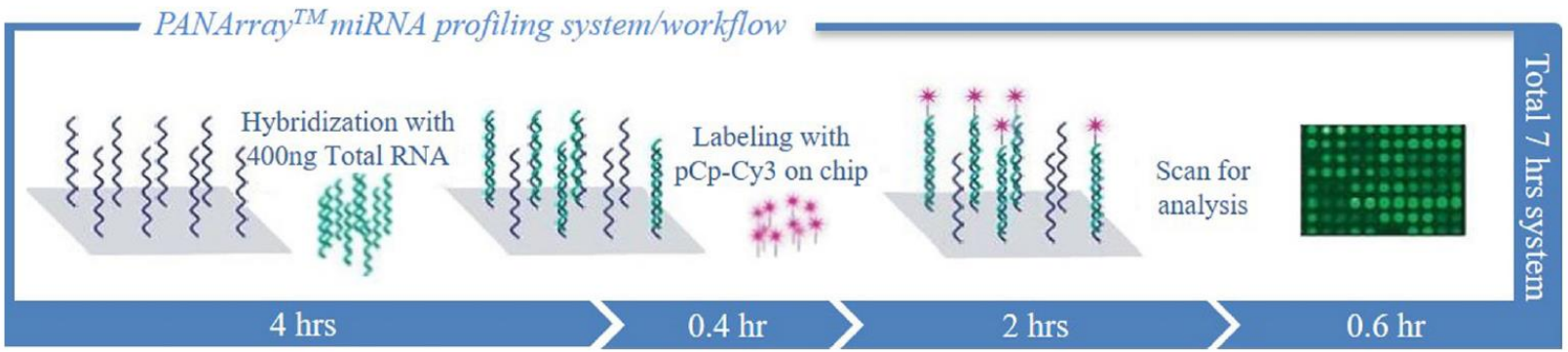


Journal of clinical microbiology (2009) 47(6):1785–1790

Jae-jin Choi, Chunhee Kim, and Heekyung Park

Won Asia Pacific Product Innovation award by Frost & Sullivan (PANArray™ HPV Chip)

PNA microarray platform for miRNA expression profiling using on-chip labeling technology

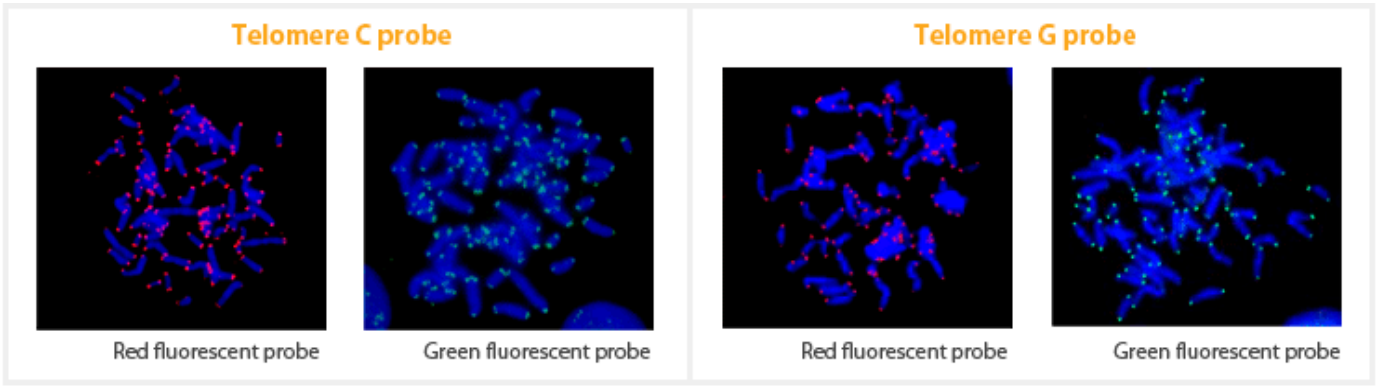


BioChip Journal (2012) 6(1):25-33 Hyunsun Kim, Jae-jin Choi, Minhye Cho & Heekyung Park

PNA FISH

PANAGENE

www.panagene.com



AdvanDx PNAFISH® (Now Opgen)

www.opgen.com

alpha laboratories
supplying quality to science

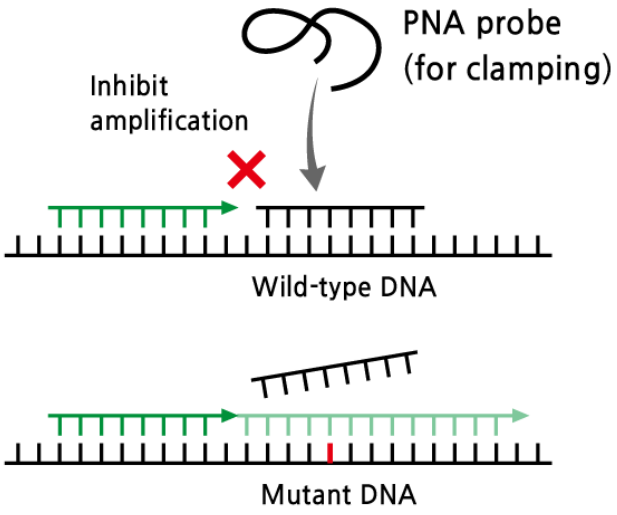
www.alphalabs.co.uk/pnafish

- **Advantage of PNA: Rapid & accurate diagnosis**

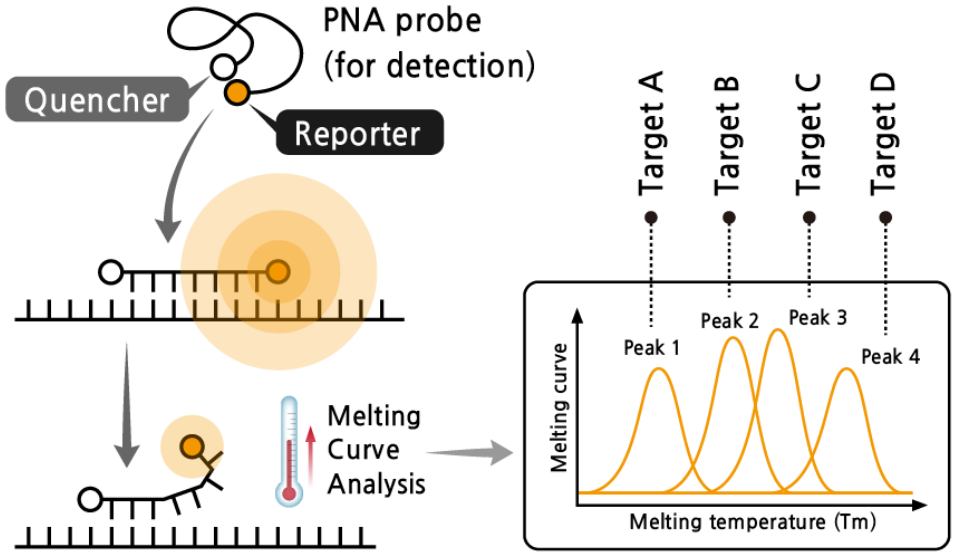
	PNA probe	DNA probe
Incubation time	~ 2 hours	Overnight

PCR-based PNA Technology

Highly Sensitive Mutation Detection (PNAClamp™ by PANAGENE)



Multiplex Detection (PANA RealTyper™ by PANAGENE)



PANAMutyper™

Sensitivity - 0.1% (somatic mutation)
Liquid Biopsy available

EGFR
- Lung

KRAS
- Colorectal
- Lung

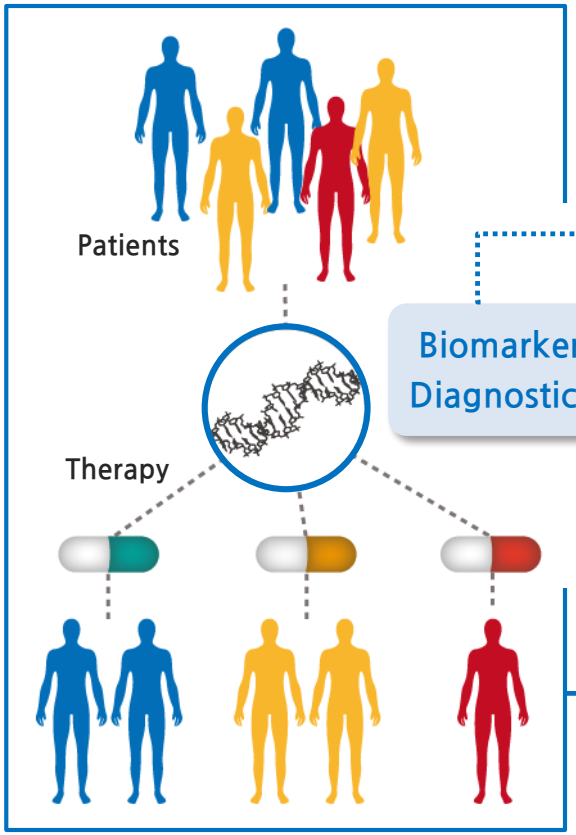
NRAS
- Melanoma
- Colorectal
- Lung

ROS1
- Lung

Tissue only

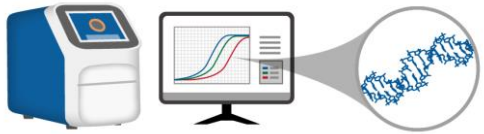
Companion Diagnostics

Personalized Medicine / Targeted Therapy



- Select optimal targeted therapy
- Minimize adverse drug effect with increase in treatment options

Molecular Diagnostics (MDx)



Analyzing biological markers in DNA/RNA to diagnose and monitor disease

Companion Diagnostics (CDx)

- Help predict drug response, reduce risk of toxicity
- CDx importance is increasing as Targeted Therapy increases (Field of breast, lung, colorectal cancer and melanoma.

"Molecular Diagnostics is essential for Patients' Treatment"

Selected PNA Production Companies

Company	Activity	Key products	Short description	Biomedical applications
Advanced Peptides	Custom PNA synthesis; PNA modifications	PNA libraries; PNA arrays	An experienced global manufacturer of custom peptides and PNAs. Their scientists have synthesized products for the scientific community for over 25 years and have met the highest standards of quality, service, and technical expertise	This activity is of interest for groups involved in synthesis of PNAs and PNA analogs
ASM Research Chemicals	Monomers for PNA synthesis	PNA monomers	A research and development organization in the field of synthesis of complex organic molecules for various applications	This activity is of interest for groups involved in PNA synthesis
Bio Synthesis		PNA FISH probes	This compa... demand PN... with different fluorophores	...therapeutic applications
Panagene	PNA synthesis; custom PNA oligomers; PNA clamp; PNA FISH probes	K-ras mutation detection kit; PNA miR inhibitors	As a biotechnology platform solution provider, it is a global leading company in molecular diagnostics and novel biomaterials	Molecular diagnosis; alteration of gene expression
PNA Bio	Custom PNA oligos; PNA FISH probes	TALEN & FN; custom PNA oligos; PNA FISH probes; PNA clamp; PNA miR inhibitors	This company offers PNA products of high quality	Molecular diagnosis; imaging; therapy
PolyOrg, Inc.	Peptide nucleic acid monomers	Modified PNA analogs	This company provides a variety of synthesis services for Life Science companies	This activity is of interest for groups involved in PNA synthesis in the fields of pharmaceuticals, biotechnology, and diagnostics

Panagene

global leading company

Roberto Gambari

Expert Opin. Ther. Patents (2014) 24(3):267-294

PNA Bio : distributor of PANAGENE

Various Patents Files Related to PNA

Table 3. Partial list of enterprises involved in recent patents or patent applications on PNAs relevant to molecular diagnosis (continued).

Patent or patent application	Title	Original assignee or co-assignee	Short description (claims)	Validity, significance, and biomedical applications
US20110111416 [94]	Peptide nucleic acid probes, kits and methods for expression profiling of microRNAs	PANAGENE	The patent describes PNA probes capable of specifically binding to a target miR through complementary to 3 – 10 base sequences in 5′ seed of the target miR	The present patent application relates to PNA probes for expression profiling of miRs. This strategy can be applied to molecular diagnosis of circulating miRs
WO2009125934 [95]	PNA probes, kits and methods for cytochrome P450 genotyping	PANAGENE	Described in this patent are PNA probes capable of genotyping a cytochrome P450 2C9, 2C19, and/or 2D6	The invention relates to the development of PNA-based probes for analysis of the expression of genes closely associated with drug metabolism
US20080248461 [96]	PNA probes, kits, and methods for detecting genotypes of human papillomavirus	PANAGENE	In this patent application PNA probes are described capable of specifically binding with selected genotypes of Human Papillomavirus (HPV) DNA	Applications are focused on the development of methods for detecting HPV genotypes by using the kits, which enables the accurate detection of all 24 genotypes of HPV found in cervix. The relevance of this method is related to the possible diagnosis of combined infection with more than one HPV genotype
US20080233557 [97]	PNA probes, kits, and methods for detecting Lamivudine-resistant Hepatitis B viruses	PANAGENE	Disclosed in this patent application are PNA probes to detect lamivudine-resistant mutants of hepatitis B virus (HBV). They can accurately detect mutations of rtL180 M, rtM204 V, rtM204I, and rtV2071 within B and C domains of HBV DNA polymerase gene, the main cause of lamivudine resistance, as well as mixed mutants of more than one mutant	The present patent application relates to molecular diagnosis of HBV, which causes acute and chronic hepatitis; the methods proposed allows the development of kits for detecting lamivudine-resistant HBV, based on PNA probes with high specificity and sensitivity
WO2011093606 [98]	Method and kit for detecting BRAF mutant using real time PCR clamping on the basis of PNA	PANAGENE	The present patent application relates to a method for detecting mutants using PNA probes which bind specifically to the wild type of codon 600 in BRAF gene	The present invention can examine tumors (such as malignant melanoma, ovarian cancer, colorectal cancer, and thyroid cancer) quickly and accurately in the early stages to enable effective treatment through early diagnosis of cancer. Similar patent applications have been filed such as WO2011105732 (Method and kit for detecting EGFR mutant detection using PNA-based real time PCR clamping) [99], WO2011049343 (Method and kit for detecting K-RAS

Expert Opin. Ther. Patents (2014) 24(3):267-294

Various Patents Files Related to PNA

Table 4. Partial list of enterprises involved in recent patents or patent applications designed for alterations of gene expression relevant for gene therapy.

Patent or patent application	Title	Original assignee or co-assignee	Short description (claims)	Validity, significance, and biomedical applications
US20100292471 [105]	Peptide nucleic acid oligomers comprising universal bases, preparation methods thereof, and kits, devices, and methods for the analysis, detection, or modulation of nucleic acids using the same	**PANAGENE**	Disclosed is a PNA oligomer with increased solubility in water and specificity upon hybridization with nucleic acids	This patent application relates to PNA oligomers with remarkably increased specificity upon hybridization with nucleic acids, allowing development of kits, devices, and methods. This permits not only highly efficient analysis and detection of nucleic acids, but also modulation of gene expression
WO2009113828 [106]	Peptide nucleic acids with good cell penetration and strong affinity for nucleic acid	**PANAGENE**	The present invention provides a novel class of PNA derivatives showing good cell penetration and strong binding affinity for nucleic acids	This patent application relates to one of the major issues in using PNAs and proposing them for molecular therapy. The claims are highly significant in the field of gene therapy
US6165720 [107]	Chemical modification of DNA using peptide nucleic acid conjugates	Gene Therapy Systems, Isis Pharmaceuticals, Inc.	Complexes comprising a nucleic acid molecule and a conjugated PNA are described in this patent. The PNA may be labeled or conjugated to proteins, peptides, carbohydrate moieties, or receptor ligands	The complexes described in this patent are used to transfect cells with plasmids, to affect their biodistribution, to promote nuclear localization, to induce transcriptional activation. The claims are highly significant in gene therapy, since the described complexes increase the efficiency of the final expression of a therapeutic gene
US5700922 [108]	PNA-DNA-PNA chimeric macromolecules	Isis Pharmaceuti-cals, Inc.	Macromolecules are provided that have increased nuclease resistance and binding affinity to a complementary strand, and that activate RNase H. The macromolecules are PNA-DNA-PNA structures, where the DNA portion is composed of subunits of 2'-deoxy-erythro-pentofuranosyl nucleotides	The molecules described in this patent are useful for diagnostics and other research purposes, including modulation of protein expression in organisms. In particular the claims are significant, since PNA-based antisense molecules do not activate RNase H
WO2002031166 [68]	Artificial transcriptional factors and methods of use	Crosslink Genetic Corp.	Artificial transcription factors (ATFs) are proposed having a non-peptidic-DNA binding domain, a flexible linker and a short synthetic effector domain	The ATFs described in this patent application are highly potent transcriptional modulators *in vitro* and *in vivo*. Methods for targeted

Expert Opin. Ther. Patents (2014) 24(3):267-294

Various Patents Files Related to PNA

Table 4. Partial list of enterprises involved in recent patents or patent applications designed for alterations of gene expression relevant for gene therapy (continued).

Patent or patent application	Title	Original assignee or co-assignee	Short description (claims)	Validity, significance, and biomedical applications
US20120183538 [126]	Sparc antisense compositions and uses thereof	Abraxis Bioscience, Llc	The invention provides SPARC antisense oligonucleotides and methods for their use in proliferative diseases such as cancer and hepatic fibrosis. Secreted protein acidic and rich in cysteine (also known as osteonectin, BM40, or SPARC) (hereainfter "SPARC") is a matrix-associated protein highly expressed in several aggressive cancers, while it is absent in the corresponding normal tissues (e.g., bladder, liver, ovary, kidney, gut, and breast)	Biomedical applications include proliferative diseases such as cancer, restenosis, fibrosis, osteoporosis, and inflammatory diseases including arthritis or exaggerated wound healing. Despite being innovative, further validation studies are necessary to understand the real impact of the proposed approach

Expert Opin. Ther. Patents (2014) 24(3):267-294

PNA-based MDx Products of PANAGENE

	Technology	Target	Disease	Development Phase	CE	KFDA
Oncology	PANAMutyper™ (Liquid biopsy)	EGFR (ver. 1)	Lung cancer	Completed	CE	
		EGFR (ver. 2)	Lung cancer	Completed		
		KRAS	Thyroid / Lung cancer	Completed	CE	
		NRAS	Colon / Lung cancer / Melanoma	Completed	CE	
		ROS1	Lung cancer	Completed	CE	
		EML4-ALK	Lung cancer	Completed	CE	
		BRAF	Thyroid / Colon cancer / Melanoma	Completed		
	PNAClamp™	EGFR	Lung cancer	Completed	CE	
		KRAS	Thyroid / Lung cancer	Completed	CE	
		NRAS	Colon / Lung cancer / Melanoma	Completed	CE	
		BRAF	Thyroid / Colon cancer / Melanoma	Completed	CE	
		PIK3CA	Breast / Colon / Lung cancer	Completed	CE	
		IDH1	Glioblastoma multiforme	Completed	CE	
		IDH2	Glioblastoma multiforme	Completed	CE	
		JAK2	Myelofibrosis / Polycythemia Vera	Completed	CE	
		BCR-ABL	Chromic myelogenous leukemia	Completed	CE	
		c-KIT	Glioblastoma / Myeloproliferative Neoplasm	Completed	CE	
		TERT	Thyroid / Lung cancer	Completed	CE	
Infectious Disease	PANA RealTyper™	HPV genotyping	Cervical cancer	Completed	CE	
		HPV screening	Cervical cancer	Completed	CE	
		STD	Sexually transmitted disease	Completed	CE	
		CRE	Resistance to antibiotic	Completed	CE	
	PANA qPCR™	TB/NTM	Tuberculosis	Completed	CE	

Search PubMed for 'EGFR' and 'PNA'

PubMed.gov

5 Cite Share
Detection of activating and acquired resistant mutation in plasma from **EGFR**-mutated NSCLC patients by peptide nucleic acid (**PNA**) clamping-assisted fluorescence melting curve analysis.
Kim CG, Shim HS, Hong MH, Cha YJ, Heo SJ, Park HS, Kim JH, Lee JG, Lee CY, Cho BC, Kim HR.
Oncotarget. 2017 May 10;8(39):65111-65122. doi: 10.18632/oncotarget.17786. eCollection 2017 Sep 12.
PMID: 29029416 Free PMC article.
A total of 102 patients with **EGFR**-mutated lung cancer were enrolled, 53 had available plasma samples at disease progression, and 28 underwent serial plasma sampling during **EGFR**-TKI treatment. ...In conclusion, PANAMutyper is reliable for detecting activating and acq ...

6 Cite Share
MassARRAY, pyrosequencing, and **PNA** clamping for **EGFR** mutation detection in lung cancer tissue and cytological samples: a multicenter study.
Min KW, Kim WS, Jang SJ, Choi YD, Chang S, Jung SH, Kim L, Roh MS, Lee CS, Shim JW, Kim MJ, Lee GK; Korean Cardiopulmonary Pathology Study Group.
J Cancer Res Clin Oncol. 2016 Oct;142(10):2209-16. doi: 10.1007/s00432-016-2211-7. Epub 2016 Aug 17.
PMID: 27535566
BACKGROUND: Testing for epidermal growth factor receptor (**EGFR**) mutation is an important process in the therapeutic plan of patients with lung cancer. ...CONCLUSIONS: When used for the detection of **EGFR** mutations, MassARRAY was more sensitive than pyrosequencing or ...

7 Cite Share
Imaging analysis of **EGFR** mutated cancer cells using peptide nucleic acid (**PNA**)-DNA probes.
Shigeto H, Ohtsuki T, Iizuka A, Akiyama Y, Yamamura S.
Analyst. 2019 Aug 7;144(15):4613-4621. doi: 10.1039/c9an00725c. Epub 2019 Jun 26.
PMID: 31241068
This study focused on the imaging analysis of a single nucleotide substitute in **EGFR** mutated cancer cells. We developed three novel peptide nucleic acid (**PNA**)-DNA probes for recognizing and detecting the following three gene mutations in **EGFR** gene mutations. ...

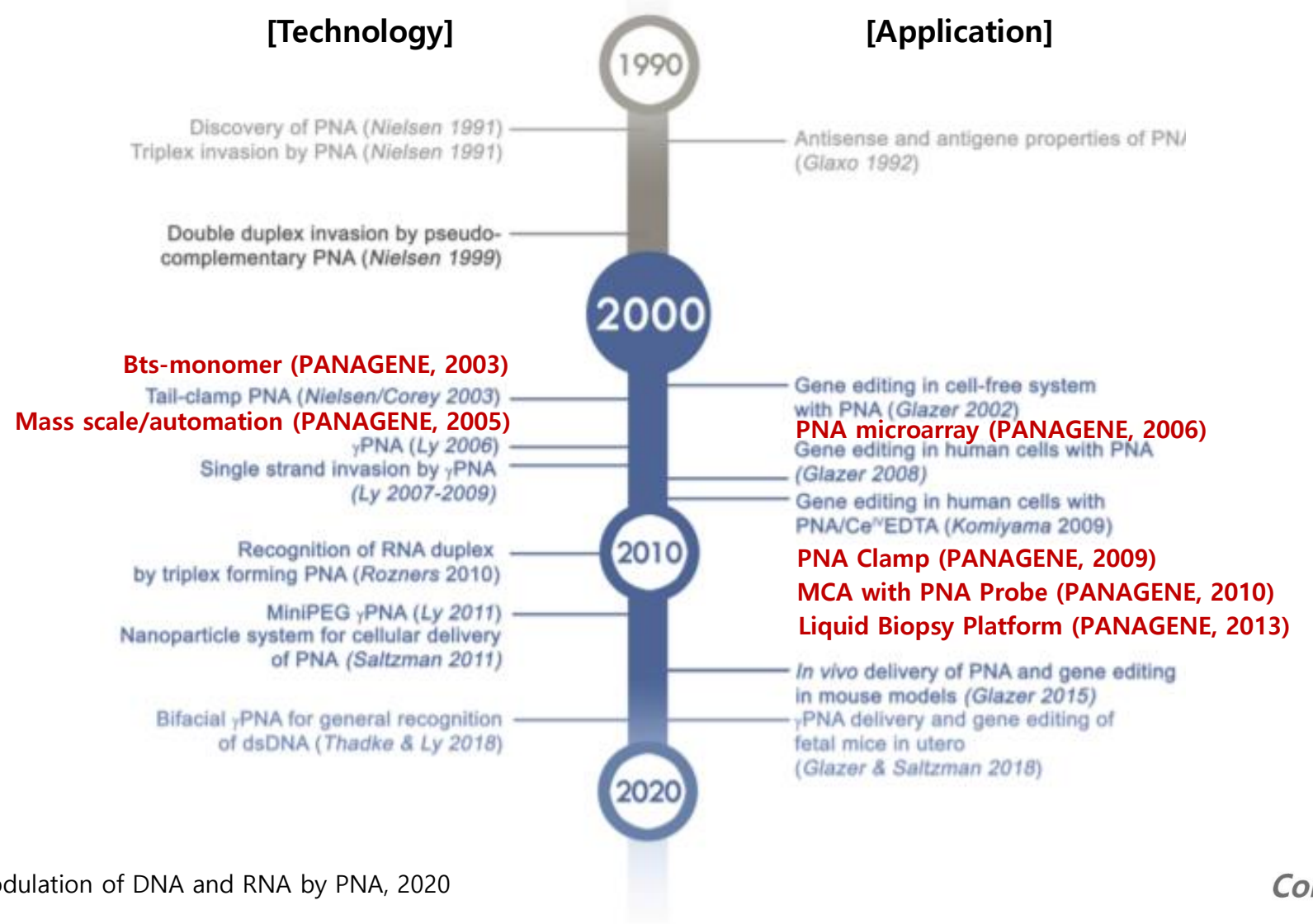
8
PNA clamping-assisted fluorescence melting curve analysis for detecting **EGFR** and KRAS mutations in the circulating tumor DNA of patients with advanced non-

- **Keyword: EGFR and PNA**
- **Total publications: 106**
- **Korean author: 34 (around 32%)**

PANAMutyper™ R EGFR for liquid biopsy

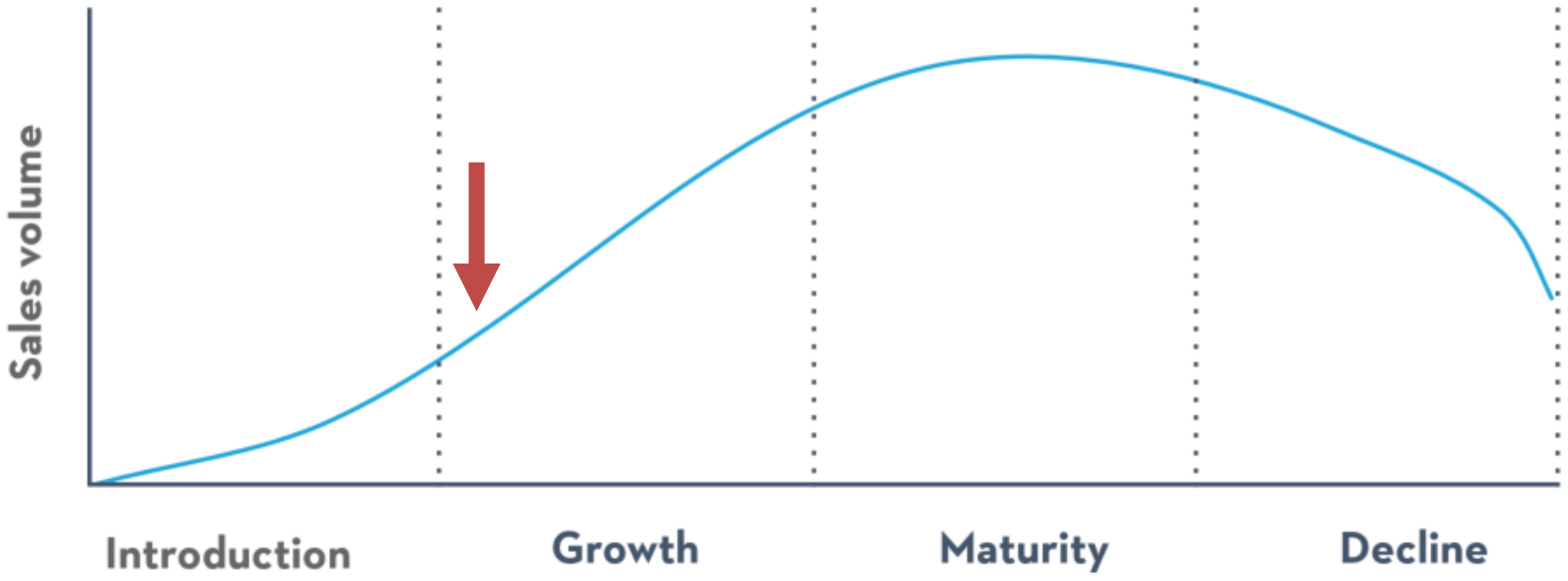
PNAClamp™ EGFR for tissue biopsy

Timeline of Important Events in the Area of PNA



Modulation of DNA and RNA by PNA, 2020

Current PNA Market Status



What phase is PNA market currently in?

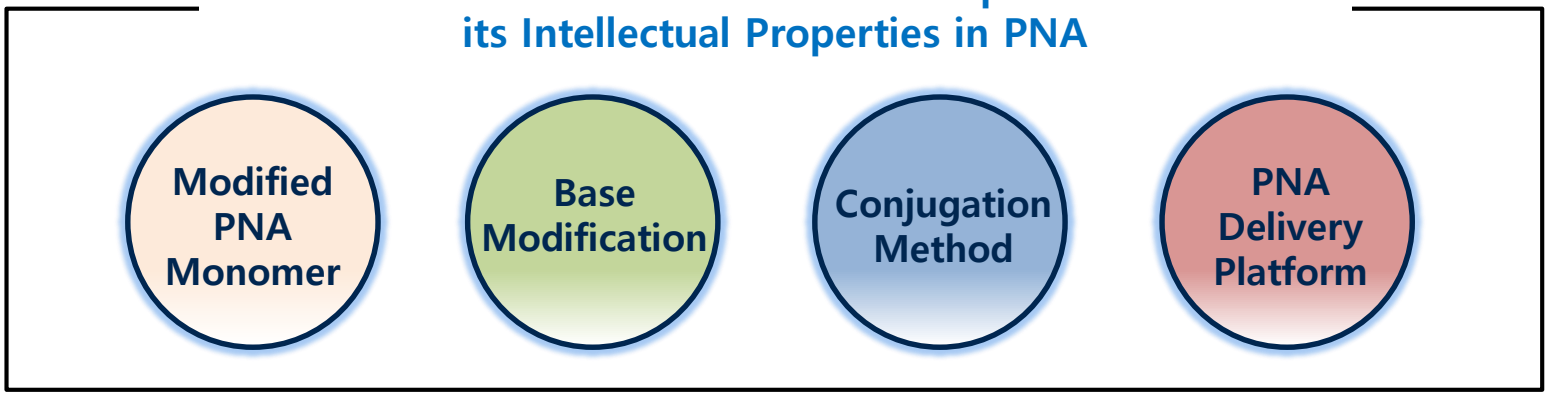
PANAGENE: The Best PNA Supplier + PNA related IP

PANAGENE will be the sole provider
for the development to Approval of PNA based therapeutics

Process	PRE-CLINICAL	INVESTIGATIONAL NEW DRUG APPLCIATION (IND)	CLINICAL TRIALS (Phase 1 ▷ 2 ▷3)	APPROVED & COMMERCIALIZED
PNA needed	nmole ~ μmole	mg ~ gram	Kg ~	Kg ~

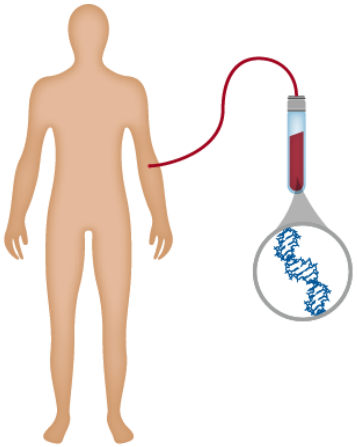
- ✓ *Secure cGMP for clinical stage supply capability*
- ✓ *Use PNA provided by PANAGENE in all process*

PANAGENE will invest on PNA related patents to secure
its Intellectual Properties in PNA



PANAGENE: Maximizing PNA-based MDx Technology

Liquid Biopsy



High sensitivity detection technology

Mutation Detection

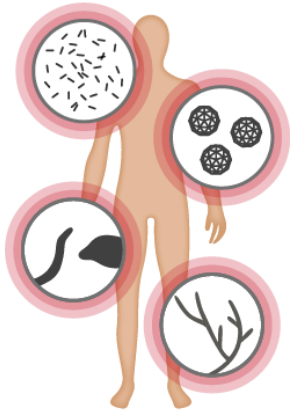
Multiplex detection technology

PNA

Quantification technology

PoCT technology

Pathogen Detection



Changing the world with PNA

PANAGENE

54, Techno 10-ro, Yuseong-gu, Daejeon, 305-510 Korea | Tel : 042-861-9295 | Fax : 042-861-9297 |
http://www.PANAGENE.com