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Supplemental Information

As Technologies for Nucleotide Therapeutics

Mature, Products Emerge

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Supplemental Table S1
TIME model statistics for RNA therapeutic technologies

Therapeutic Technologies

Technology	PubMed Search	T_I	T_G	T_E	Nerr_ModelAvg	T_E_err
ONTs	antisense oligonucleotides OR "ribozyme" OR (("rna interference") OR "rna interference"[MeSH Terms])	1972.7	1988.2	2003.8	0.07	0.5
ASO	antisense oligonucleotides	1979.8	1987.6	1995.4	0.04	0.2
RNAi	"rna interference" OR "rna interference"[MeSH Terms]	1991.1	1998.5	2006.0	0.16	0.6
Ribozyme	"ribozyme"	1980.1	1988.1	1996.0	0.04	0.2
Aptamer	rna aptamer or dna aptamer	1986.2	1999.5	2012.9	0.07	0.4
siRNA	"small interfering"[MeSH Terms] OR "short interfering rna"[All Fields]	1994.4	2000.1	2005.9	0.1	0.4
miRNA	microrna	N/A	N/A	N/A	N/A	N/A
CRISPR	crispr	N/A	N/A	N/A	N/A	N/A

Chemistry Technologies

Technology	PubMed Search	T_I	T_G	T_E	Nerr_ModelAvg	T_E_err
phosphorodiamidate morpholino oligomers	phosphorodiamidate morpholino oligomers	N/A	N/A	N/A	N/A	N/A
phosphorothioate oligonucleotides	phosphorothioate oligonucleotides	1982.1	1988.6	1995.1	0.06	0.4
LNA	locked nucleic acids	1988.2	1997.9	2007.7	0.03	0.2
2'-OME	2'-O-methoxyethyl OR 2'-MOE OR 2'-O-alkyl	1988.7	1995.7	2002.7	0.07	0.6

Molecular Target Technologies

Technology	PubMed Search	T_I	T_G	T_E	Nerr_ModelAvg	T_E_err	Therapeutic	Therapeutic Approval Year	Therapeutic Technology
CMV_IE2	cytomegalovirus ul123 OR cytomegalovirus ie2	1979.7	1988.4	1997.2	0.06	0.5	fomivirsen	1998	ASO
IRS 1	insulin receptor substrate 1	1975.8	1987.4	1999.0	0.07	0.5			ASO
CSF 2	colony stimulating factor 2	1971.9	1981.0	1990.2	0.08	0.5			ASO
SMAD 7	smad 7	1988.9	1997.9	2007.0	0.13	0.7			ASO
Transthyretin	transthyretin	N/A	N/A	N/A	N/A	N/A			RNAi/ASO

p53	tumor protein p53	1973.6	1985.5	1997.4	0.13	0.7			RNAi/ASO
Clusterin	clusterin	1966.5	1984.8	2003.1	0.15	1.5			ASO
SMN 2	((survival motor neuron 2) OR smn2) OR "survival motor neuron protein 2"[MeSH Terms]	1967.4	1986.4	2005.3	0.02	0.2	nusinersen	2016	ASO
Dystrophin	dystrophin	1968.9	1981.9	1995.0	0.15	1.3	eteplirsen	2016	ASO
Toll-like receptor 9	toll-like receptor 9	1994.2	2000.7	2007.1	0.09	0.4			ASO
Fms-like tyrosine kinase	fms-like tyrosine kinase-1	1992.8	2001.7	2010.6	0.07	0.4			Ribozyme/RNAi
Telomerase rna component	telomerase rna component	1987.1	1993.4	1999.7	0.14	0.8			Ribozyme
VEGF	vegf-a	1981.3	1991.9	2002.5	0.06	0.3	pegaptanib	2004	aptamer/RNAi/ASO
Bcl-2	bcl-2	1975.9	1987.6	1999.3	0.14	0.8			RNAi/ASO
PKC_alpha	protein kinase c alpha	1978.9	1988.7	1998.5	0.06	0.4			ASO
TGF beta 2	transforming growth factor beta 2	1979.6	1989.4	1999.2	0.09	0.6			ASO
Caspase 2	caspase 2	1987.5	1994.8	2002.2	0.07	0.4			RNAi
nf kappa b p65	nf kappa b p65	1979.6	1993.4	2007.1	0.08	0.6			ASO
Apolipoprotein ciii	apolipoprotein ciii	1959.9	1975.1	1990.4	0.09	1.0			RNAi/ASO
Apolipoprotein b-100	apolipoprotein b-100	1973.4	1983.7	1994.0	0.07	0.6	mipomersen	2003	RNAi/ASO
PDGFR	platelet-derived growth factor receptor	1963.1	1980.0	1996.8	0.13	1.1			Aptamer
Complement component 5	complement component 5	1953.9	1967.6	1981.3	0.09	0.9			Aptamer
Coagulation factor IX	coagulation factor IX	1924.3	1957.2	1990.2	0.04	0.6			Aptamer