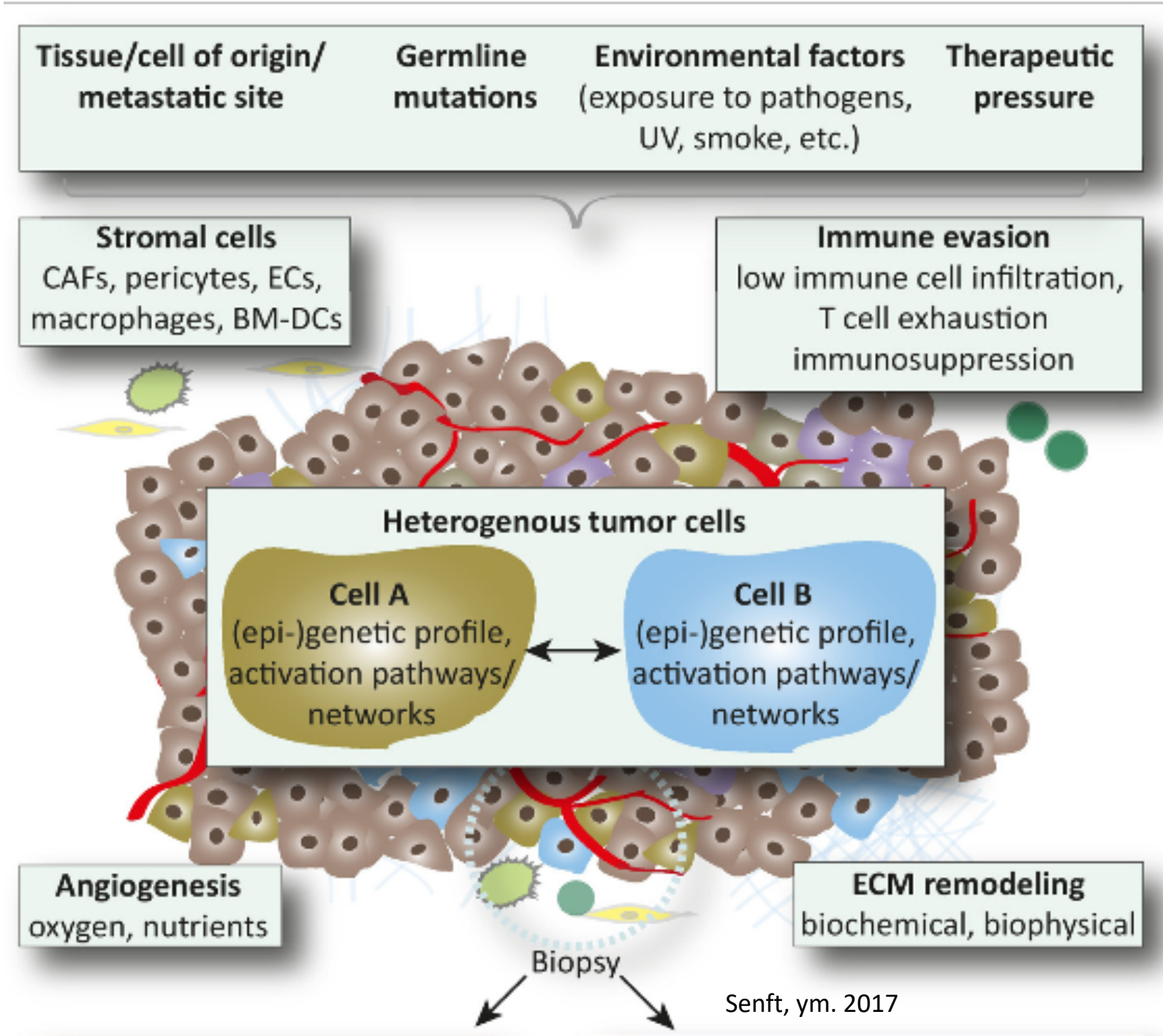
YKSILÖLLISEN SYÖVÄNHOIDON MALLIMAA 2020

Syövän molekyyliprofilointi

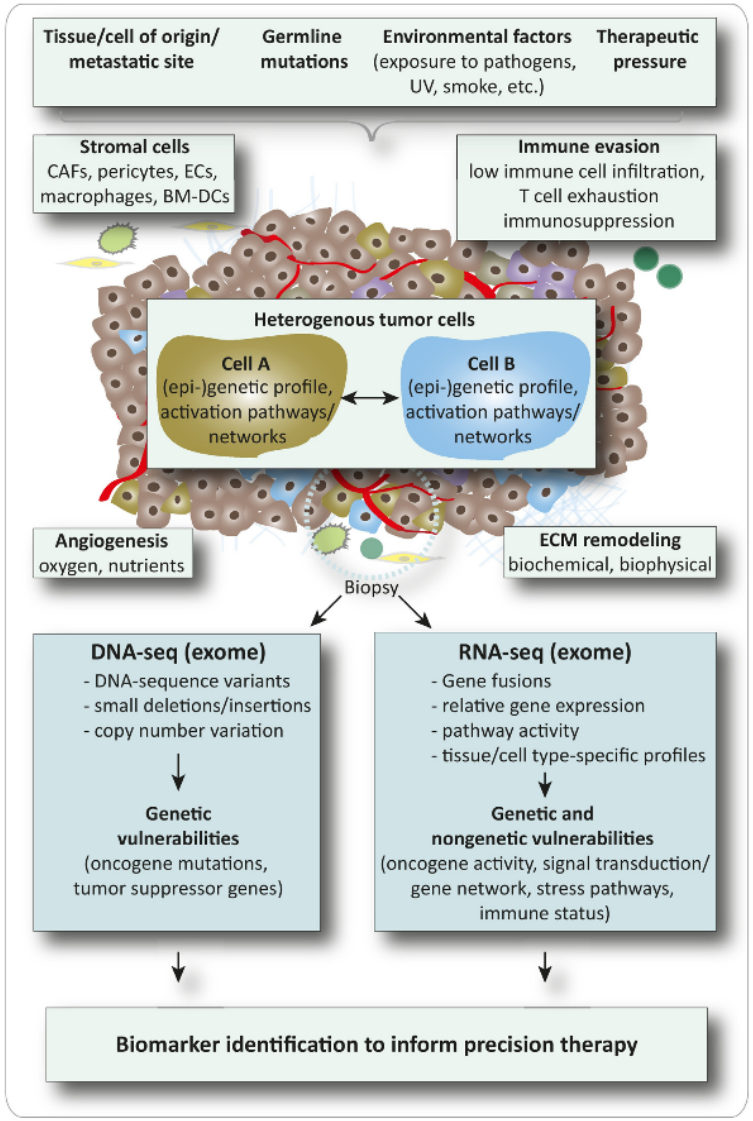
- Arto Mannermaa
  - Itä-Suomen yliopisto
  - Itä-Suomen Biopankki
  - arto.mannermaa@uef.fi

Syövän molekyyliprofilointi, miksi?



Senft, ym. 2017

Syövän molekyyliprofilointi, miksi?



Senft, ym. 2017

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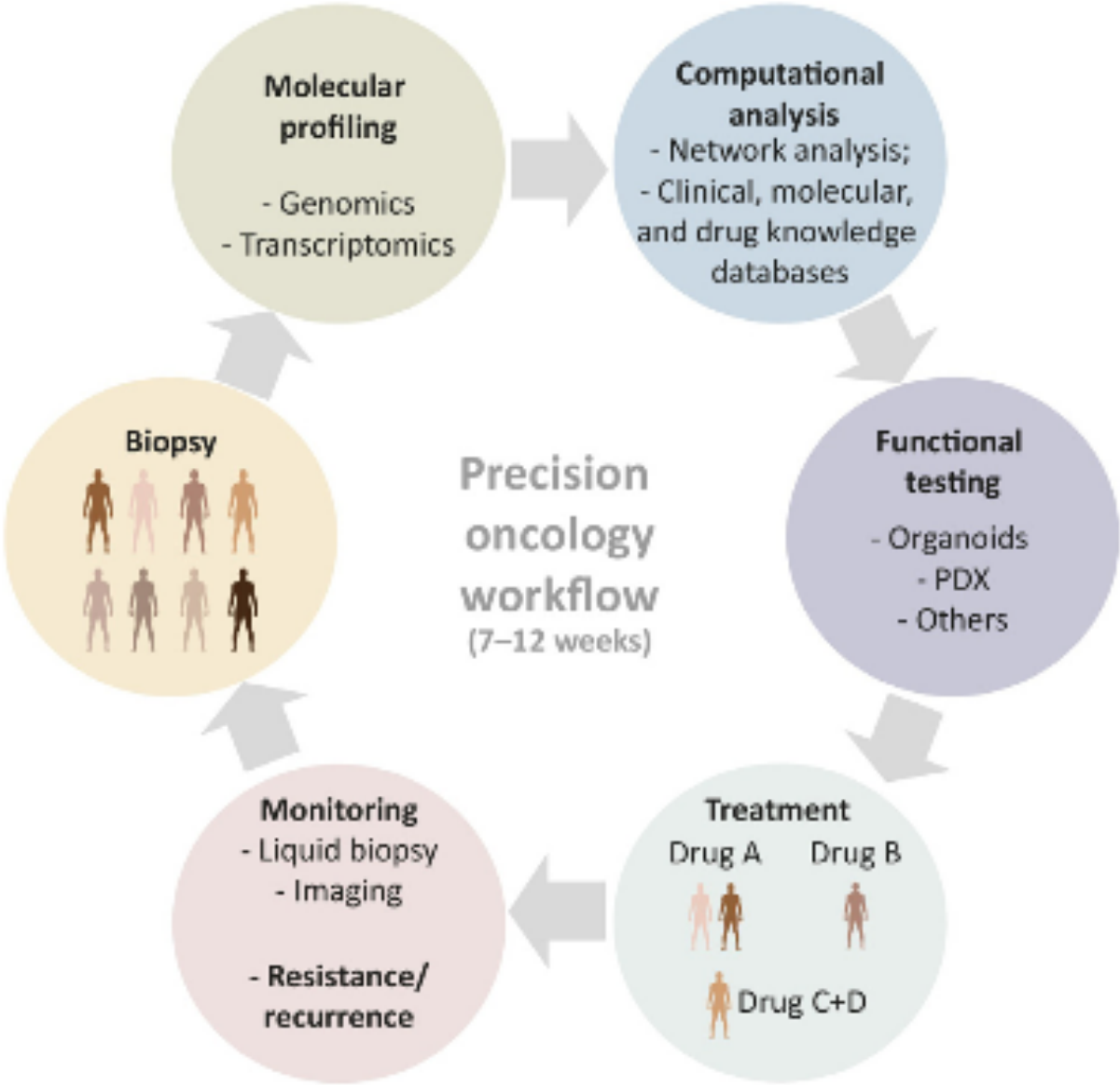
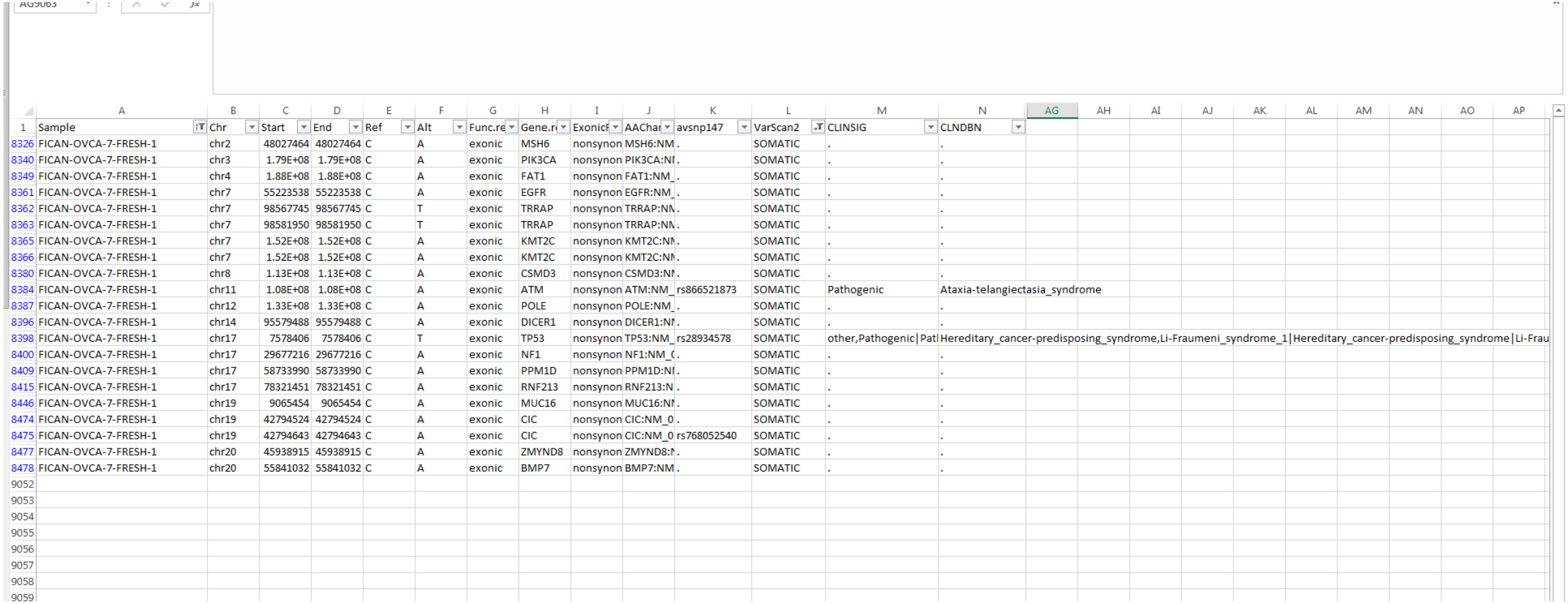
Miten?



Trends in Molecular Medicine

YKSILÖLLISEN SYÖVÄNHOIDON MALLIMAA 2020

Kuopio, FICAN-EAST-pilotti



	A	B	C	D	E	F	G	H	I	J	K	L	M	N	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP
1	Sample	Chr	Start	End	Ref	Alt	Func.re	Gene.re	Exonic	AAChar	avsnp147	VarScan2	CLINSIG	CLNDBN										
8326	FICAN-OVCA-7-FRESH-1	chr2	48027464	48027464	C	A	exonic	MSH6	nonsynon	MSH6:NM	.	SOMATIC	.	.										
8340	FICAN-OVCA-7-FRESH-1	chr3	1.79E+08	1.79E+08	C	A	exonic	PIK3CA	nonsynon	PIK3CA:NI	.	SOMATIC	.	.										
8349	FICAN-OVCA-7-FRESH-1	chr4	1.88E+08	1.88E+08	C	A	exonic	FAT1	nonsynon	FAT1:NM_	.	SOMATIC	.	.										
8361	FICAN-OVCA-7-FRESH-1	chr7	55223538	55223538	C	A	exonic	EGFR	nonsynon	EGFR:NM_	.	SOMATIC	.	.										
8362	FICAN-OVCA-7-FRESH-1	chr7	98567745	98567745	C	T	exonic	TRRAP	nonsynon	TRRAP:NM	.	SOMATIC	.	.										
8363	FICAN-OVCA-7-FRESH-1	chr7	98581950	98581950	C	T	exonic	TRRAP	nonsynon	TRRAP:NM	.	SOMATIC	.	.										
8365	FICAN-OVCA-7-FRESH-1	chr7	1.52E+08	1.52E+08	C	A	exonic	KMT2C	nonsynon	KMT2C:NM	.	SOMATIC	.	.										
8366	FICAN-OVCA-7-FRESH-1	chr7	1.52E+08	1.52E+08	C	A	exonic	KMT2C	nonsynon	KMT2C:NM	.	SOMATIC	.	.										
8380	FICAN-OVCA-7-FRESH-1	chr8	1.13E+08	1.13E+08	C	A	exonic	CSMD3	nonsynon	CSMD3:NM	.	SOMATIC	.	.										
8384	FICAN-OVCA-7-FRESH-1	chr11	1.08E+08	1.08E+08	C	A	exonic	ATM	nonsynon	ATM:NM_	rs866521873	SOMATIC	Pathogenic	Ataxia-telangiectasia_syndrome										
8387	FICAN-OVCA-7-FRESH-1	chr12	1.33E+08	1.33E+08	C	A	exonic	POLE	nonsynon	POLE:NM_	.	SOMATIC	.	.										
8396	FICAN-OVCA-7-FRESH-1	chr14	95579488	95579488	C	A	exonic	DICER1	nonsynon	DICER1:NM	.	SOMATIC	.	.										
8398	FICAN-OVCA-7-FRESH-1	chr17	7578406	7578406	C	T	exonic	TP53	nonsynon	TP53:NM_	rs28934578	SOMATIC	other,Pathogenic|Pat	Hereditary_cancer-predisposing_syndrome,Li-Fraumeni_syndrome_1|Hereditary_cancer-predisposing_syndrome|Li-Frau										
8400	FICAN-OVCA-7-FRESH-1	chr17	29677216	29677216	C	A	exonic	NF1	nonsynon	NF1:NM_(	.	SOMATIC	.	.										
8409	FICAN-OVCA-7-FRESH-1	chr17	58733990	58733990	C	A	exonic	PPM1D	nonsynon	PPM1D:NI	.	SOMATIC	.	.										
8415	FICAN-OVCA-7-FRESH-1	chr17	78321451	78321451	C	A	exonic	RNF213	nonsynon	RNF213:N	.	SOMATIC	.	.										
8446	FICAN-OVCA-7-FRESH-1	chr19	9065454	9065454	C	A	exonic	MUC16	nonsynon	MUC16:NI	.	SOMATIC	.	.										
8474	FICAN-OVCA-7-FRESH-1	chr19	42794524	42794524	C	A	exonic	CIC	nonsynon	CIC:NM_0	.	SOMATIC	.	.										
8475	FICAN-OVCA-7-FRESH-1	chr19	42794643	42794643	C	A	exonic	CIC	nonsynon	CIC:NM_0	rs768052540	SOMATIC	.	.										
8477	FICAN-OVCA-7-FRESH-1	chr20	45938915	45938915	C	A	exonic	ZMYND8	nonsynon	ZMYND8:N	.	SOMATIC	.	.										
8478	FICAN-OVCA-7-FRESH-1	chr20	55841032	55841032	C	A	exonic	BMP7	nonsynon	BMP7:NM	.	SOMATIC	.	.										
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SYÖVÄNHOIDON
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Löydösten analyysi

78

CC:Patients with breast cancer and the CC genotype may have an increased risk of developing neutropenia when treated with cyclophosphamide, epirubicin and fluorouracil as compared to patients with the CT or TT genotypes. Other genetic also affect a patient's risk of developing neutropenia.,"CT:Patients with breast cancer and the CT genotype may have an increased risk of developing neutropenia when treated with cyclophosphamide, epirubicin and fluorouracil as compared genotype, but a decreased risk compared to patients with the CC genotype. Other genetic and clinical factors may also affect a patient's risk of developing neutropenia.","TT:Patients with breast cancer and the TT genotype may have a decreas neutropenia when treated with cyclophosphamide, epirubicin and fluorouracil as compared to patients with the CC or CT genotypes. Other genetic and clinical factors may also affect a patient's risk of developing neutropenia."

A	B	C	D	E	G	H	I	J	K	L	P	Q	R	S
Clinical Annotation ID	Location	Gene	Level of Evi	Clinical Annotation	Annotation Text	Variant Ar	Variant Ar	Literature	Evidence	Related Chemicals				
1449167200	rs12302749	SPSB2 (PA142670872)	4	Efficacy	CC:Patients with the CC genotype and Att	1.45E+09	Allele C is	15100124	1	methylphenidate (PA450464)				
1449167211	rs10420097	ZNF211 (PA37582)	4	Efficacy	AA:Patients with the AA genotype and Att	1.45E+09	Allele G is	15100124	1	methylphenidate (PA450464)				
1449167228	rs3810818	CORO7 (PA134910806)	4	Efficacy	AA:Patients with the AA genotype and Att	1.45E+09	Allele A is	15100124	1	methylphenidate (PA450464)				
1449167245	rs2886059	ALDH1L1 (PA28393)	4	Efficacy	AA:Patients with the AA genotype and Att	1.45E+09	Allele C is	15100124	1	methylphenidate (PA450464)				
1449167256	rs9901675	FXR2 (PA28440)	4	Efficacy	AA:Patients with the AA genotype and Att	1.45E+09	Allele A is	15100124	1	methylphenidate (PA450464)				
1449167267	rs4805162	ZNF565 (PA134970652)	4	Efficacy	AA:Patients with the AA genotype and Att	1.45E+09	Allele G is	15100124	1	methylphenidate (PA450464)				
1449167278	rs4562	ELP5 (PA143485405)	4	Efficacy	AA:Patients with the AA genotype and Att	1.45E+09	Allele A is	15100124	1	methylphenidate (PA450464)				
1449716056	rs2275913	IL17A (PA29794)	3	Dosage	AA:Patients with the AA genotype may re	1.45E+09	Allele A is	15101063	1	opioids (PA452618)				
1448636695	rs35599367	CYP3A4 (PA130)	3	Metabolism/PK	AG:Patients with the AG genotype and me	1.45E+09	Genotype	15099039	1	everolimus (PA164746311)				
1449716178	rs9397685	OPRM1 (PA31945)	3	Toxicity/ADR	AA:Patients with the AA genotype may ex	1.45E+09	Genotype	15101065	1	fentanyl (PA449599)				
1449716207	rs13093031		3	Efficacy	AA:Patients with the AA genotype may ha	1.45E+09	Genotype	15101066	1	fentanyl (PA449599)				
1449191379	rs368505753	CFTR (PA109)	1A	Efficacy	CC:Patients with the CC genotype (do not	1.45E+09	Allele T is	15061453	1	ivacaftor (PA165950341)				
1449191385	rs115545701	CFTR (PA109)	1A	Efficacy	CC:Patients with the CC genotype (do not	1.45E+09	Allele T is	15061453	1	ivacaftor (PA165950341)				
1449191395	rs121908751	CFTR (PA109)	4	Efficacy	AA:Patients with the AA genotype (two cc	1.45E+09	Allele A is	15061453	1	ivacaftor (PA165950341)				
1449191401	rs397508537	CFTR (PA109)	1A	Efficacy	AA:Patients with the AA genotype (two cc	1.45E+09	Allele A is	15061453	1	ivacaftor (PA165950341)				
1449191407	rs113993958	CFTR (PA109)	1A	Efficacy	CC:Patients with the CC genotype (two co	1.45E+09	Allele C is	15061453	1	ivacaftor (PA165950341)				
1449191413	rs77834169	CFTR (PA109)	1A	Efficacy	CC:Patients with the CC genotype (do not	1.45E+09	Allele T is	15061453	1	ivacaftor (PA165950341)				
1449191424	rs397508759	CFTR (PA109)	1A	Efficacy	AA:Patients with the AA genotype (two cc	1.45E+09	Allele A is	15061453	1	ivacaftor (PA165950341)				
1449191430	rs121908752	CFTR (PA109)	1A	Efficacy	GG:Patients with the GG genotype (two cc	1.45E+09	Allele G is	15061453	1	ivacaftor (PA165950341)				
1449270967	rs4968187	TP53 (PA36679)	3	Toxicity/ADR	CC:Patients with breast cancer and the CC	1.45E+09	Allele T is	15100599	1	cyclophosphamide (PA449165),"epirubicin (PA449476)","fluorouracil (PA128406956)"				
1449191367	rs397508328	CFTR (PA109)	4	Efficacy	AA:Patients with the AA genotype (do not	1.45E+09	Allele G is	15061453	1	ivacaftor (PA165950341)				
1449163934	rs762551	CYP1A2 (PA27093)	3	Metabolism/PK	AA:Patients with the AA genotype may ha	827617207	Genotype	7252003,8	4	caffeine (PA448710)				
1449169484	rs7668258	UGT2B7 (PA361)	3	Metabolism/PK	CC:Patients with the CC genotype and epi	827812755	Genotype	14790059,	4	valproic acid (PA451846)				
1449169546	rs11568732	CYP2C19 (PA124)	3	Toxicity/ADR	GG:The GG genotype is associated with an	1.45E+09	Allele G is	15100113	1	clopidogrel (PA449053)				
1449169601	rs1799722	BDKRB2 (PA80)	3	Metabolism/PK	CC:Subjects with the CC genotype may hav	1.45E+09	Genotype	15100205	1	atorvastatin (PA448500)				
1449169675	rs1105879	UGT1A6 (PA37181)	4	Efficacy	AA:Patients with the AA genotype may be	1.45E+09	Genotype	15100203	1	aspirin (PA448497)				
1449564720	rs7270101	ITPA (PA29973)	3	Dosage,"Toxicity/A	AA:Patients with precursor cell lymphobla	1.45E+09	Genotype	15096664	1	mercaptopurine (PA450379),"methotrexate (PA450428)"				
1449566673	rs4979223	SLC31A1 (PA118)	3	Efficacy,"Toxicity/A	AA:Patients with the AA genotype and no	144956634	Genotype	15100865	2	Platinum compounds (PA164713176)				
1449566679	rs4978536	SLC31A1 (PA118)	3	Toxicity/ADR	AA:Patients with the AA genotype and no	1.45E+09	Genotype	15100865	1	Platinum compounds (PA164713176)				
1449566685	rs2233914	SLC31A1 (PA118)	3	Efficacy,"Toxicity/A	AA:Patients with the AA genotype and no	144956643	Genotype	15100865	2	Platinum compounds (PA164713176)				

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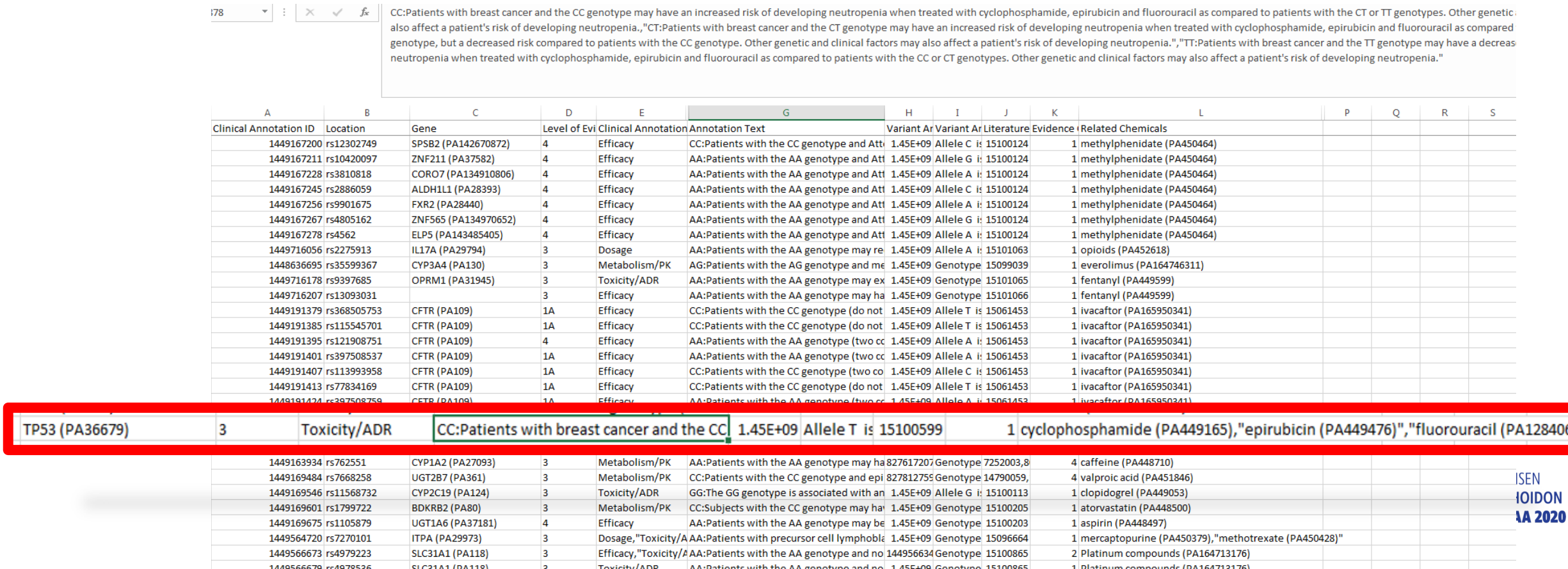

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Clinical Annotation ID	Location	Gene	Level of Evi	Clinical Annotation	Annotation Text	Variant Ar	Variant Ar	Literature	Evidence	Related Chemicals
1449167200	rs12302749	SPSB2 (PA142670872)	4	Efficacy	CC:Patients with the CC genotype and Att	1.45E+09	Allele C is	15100124	1	methylphenidate (PA450464)
1449167211	rs10420097	ZNF211 (PA37582)	4	Efficacy	AA:Patients with the AA genotype and Att	1.45E+09	Allele G is	15100124	1	methylphenidate (PA450464)
1449167228	rs3810818	CORO7 (PA134910806)	4	Efficacy	AA:Patients with the AA genotype and Att	1.45E+09	Allele A is	15100124	1	methylphenidate (PA450464)
1449167245	rs2886059	ALDH1L1 (PA28393)	4	Efficacy	AA:Patients with the AA genotype and Att	1.45E+09	Allele C is	15100124	1	methylphenidate (PA450464)
1449167256	rs9901675	FXR2 (PA28440)	4	Efficacy	AA:Patients with the AA genotype and Att	1.45E+09	Allele A is	15100124	1	methylphenidate (PA450464)
1449167267	rs4805162	ZNF565 (PA134970652)	4	Efficacy	AA:Patients with the AA genotype and Att	1.45E+09	Allele G is	15100124	1	methylphenidate (PA450464)
1449167278	rs4562	ELP5 (PA143485405)	4	Efficacy	AA:Patients with the AA genotype and Att	1.45E+09	Allele A is	15100124	1	methylphenidate (PA450464)
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1448636695	rs35599367	CYP3A4 (PA130)	3	Metabolism/PK	AG:Patients with the AG genotype and me	1.45E+09	Genotype	15099039	1	everolimus (PA164746311)
1449716178	rs9397685	OPRM1 (PA31945)	3	Toxicity/ADR	AA:Patients with the AA genotype may ex	1.45E+09	Genotype	15101065	1	fentanyl (PA449599)
1449716207	rs13093031		3	Efficacy	AA:Patients with the AA genotype may ha	1.45E+09	Genotype	15101066	1	fentanyl (PA449599)
1449191379	rs368505753	CFTR (PA109)	1A	Efficacy	CC:Patients with the CC genotype (do not	1.45E+09	Allele T is	15061453	1	ivacaftor (PA165950341)
1449191385	rs115545701	CFTR (PA109)	1A	Efficacy	CC:Patients with the CC genotype (do not	1.45E+09	Allele T is	15061453	1	ivacaftor (PA165950341)
1449191395	rs121908751	CFTR (PA109)	4	Efficacy	AA:Patients with the AA genotype (two cc	1.45E+09	Allele A is	15061453	1	ivacaftor (PA165950341)
1449191401	rs397508537	CFTR (PA109)	1A	Efficacy	AA:Patients with the AA genotype (two cc	1.45E+09	Allele A is	15061453	1	ivacaftor (PA165950341)
1449191407	rs113993958	CFTR (PA109)	1A	Efficacy	CC:Patients with the CC genotype (two co	1.45E+09	Allele C is	15061453	1	ivacaftor (PA165950341)
1449191413	rs77834169	CFTR (PA109)	1A	Efficacy	CC:Patients with the CC genotype (do not	1.45E+09	Allele T is	15061453	1	ivacaftor (PA165950341)
TP53 (PA36679)	3	Toxicity/ADR	CC:Patients with breast cancer and the CC	1.45E+09	Allele T is	15100599	1	cyclophosphamide (PA449165),"epirubicin (PA449476)","fluorouracil (PA128406956)"		
1449163934	rs762551	CYP1A2 (PA27093)	3	Metabolism/PK	AA:Patients with the AA genotype may ha	827617207	Genotype	7252003,8	4	caffeine (PA448710)
1449169484	rs7668258	UGT2B7 (PA361)	3	Metabolism/PK	CC:Patients with the CC genotype and epi	827812755	Genotype	14790059,	4	valproic acid (PA451846)
1449169546	rs11568732	CYP2C19 (PA124)	3	Toxicity/ADR	GG:The GG genotype is associated with an	1.45E+09	Allele G is	15100113	1	clopidogrel (PA449053)
1449169601	rs1799722	BDKRB2 (PA80)	3	Metabolism/PK	CC:Subjects with the CC genotype may ha	1.45E+09	Genotype	15100205	1	atorvastatin (PA448500)
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1449564720	rs7270101	ITPA (PA29973)	3	Dosage,"Toxicity/A	AA:Patients with precursor cell lymphobla	1.45E+09	Genotype	15096664	1	mercaptopurine (PA450379),"methotrexate (PA450428)"
1449566673	rs4979223	SLC31A1 (PA118)	3	Efficacy,"Toxicity/A	AA:Patients with the AA genotype and no	144956634	Genotype	15100865	2	Platinum compounds (PA164713176)

ISEN
HOIDON
AA 2020

Molekyyliprofilointi/KUH

- Profilointitulokset tulkitaan moniammatillisessa ryhmässä, jotta biologisesta tiedosta saadaan hoitoa edistävää tietoa
- Työryhmän toimintaa pilotoidaan syksyn 2018 aikana
- Monipuolisen tiedon yhdistäminen on täsmälääketieteen edellytys!

Molekyyliprofilointi/Lääkekehitys

- Syöpäsairaudet ovat toimineet täsmälääkkeiden kehittämisen menestyksekkäänä koekenttänä, suuri osa lääkekehitysprojekteista kohdistuu syöpään.
- Potilaskohtaiset profiloinnit ja yksilölliset hoidot edistävät oikeiden hoitojen antamista oikeille potilaille ja sitä kautta tehostavat terveydenhuoltoa

Kallioniemi & Mäkelä, 2017

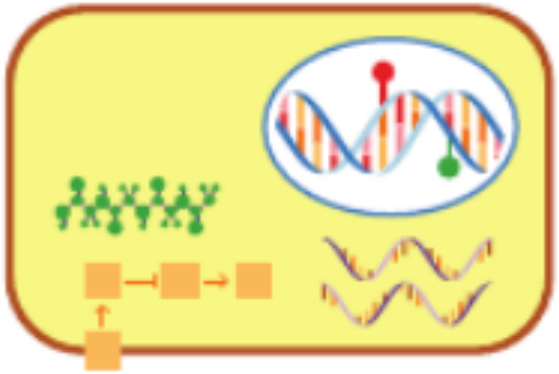
Tulevaisuus

PanCancer Atlas

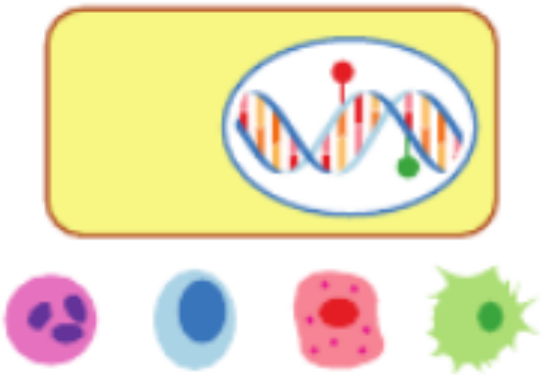
Substrates

DNA

DNA, RNA & Protein



Cellular



Associations

Germline & somatic	Driver & molecular subtypes	Immune cell & tumor

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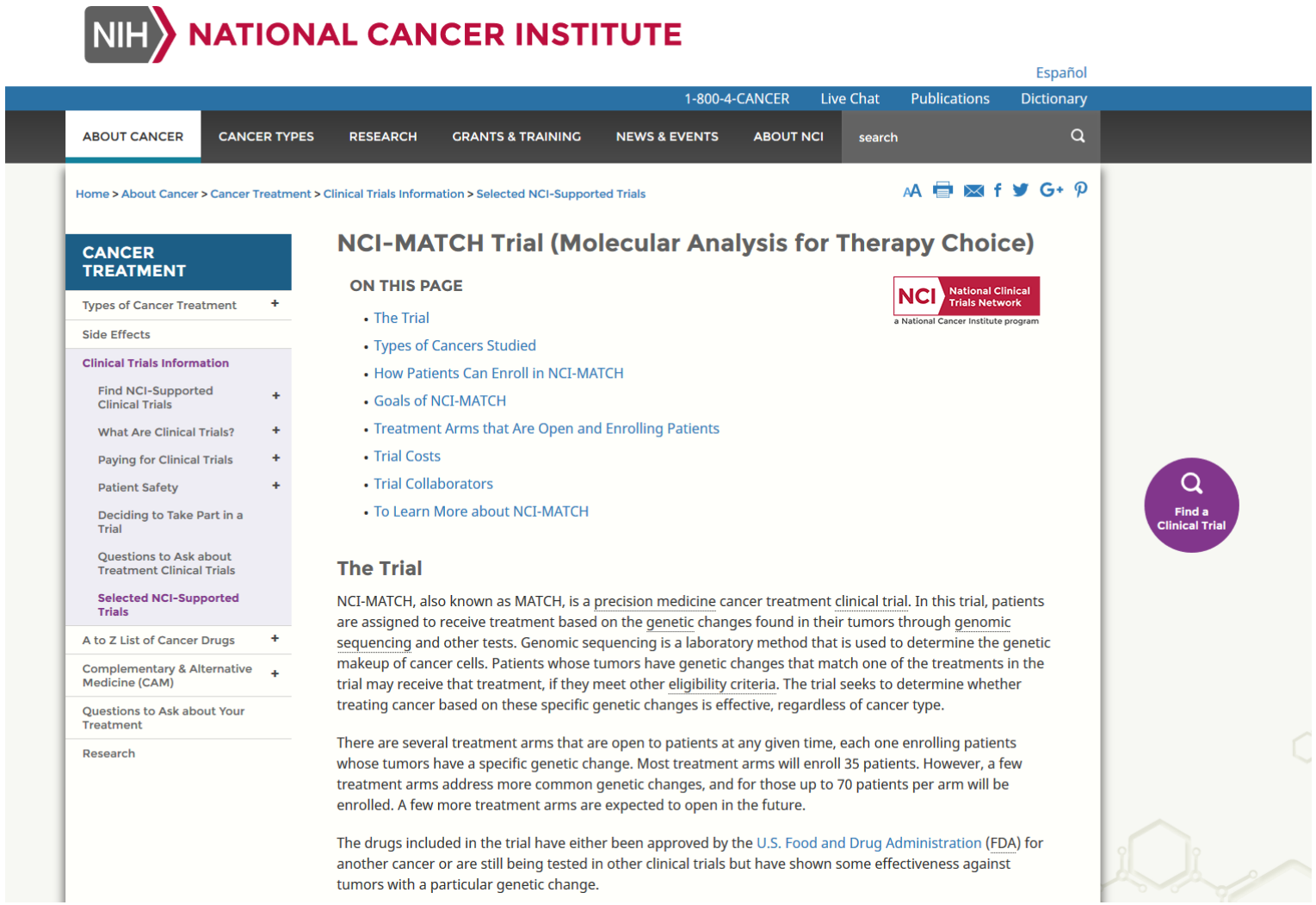
Kliininen käyttö edellyttää tutkimustietoa



NIH NATIONAL CANCER INSTITUTE

Español

1-800-4-CANCER Live Chat Publications Dictionary

ABOUT CANCER | CANCER TYPES | RESEARCH | GRANTS & TRAINING | NEWS & EVENTS | ABOUT NCI | search

Home > About Cancer > Cancer Treatment > Clinical Trials Information > Selected NCI-Supported Trials

CANCER TREATMENT

- Types of Cancer Treatment +
- Side Effects
- Clinical Trials Information
  - Find NCI-Supported Clinical Trials +
  - What Are Clinical Trials? +
  - Paying for Clinical Trials +
  - Patient Safety +
  - Deciding to Take Part in a Trial
  - Questions to Ask about Treatment Clinical Trials
  - Selected NCI-Supported Trials
- A to Z List of Cancer Drugs +
- Complementary & Alternative Medicine (CAM) +
- Questions to Ask about Your Treatment
- Research

NCI-MATCH Trial (Molecular Analysis for Therapy Choice)

NCI National Clinical Trials Network
a National Cancer Institute program

ON THIS PAGE

- The Trial
- Types of Cancers Studied
- How Patients Can Enroll in NCI-MATCH
- Goals of NCI-MATCH
- Treatment Arms that Are Open and Enrolling Patients
- Trial Costs
- Trial Collaborators
- To Learn More about NCI-MATCH

Find a Clinical Trial

The Trial

NCI-MATCH, also known as MATCH, is a precision medicine cancer treatment clinical trial. In this trial, patients are assigned to receive treatment based on the genetic changes found in their tumors through genomic sequencing and other tests. Genomic sequencing is a laboratory method that is used to determine the genetic makeup of cancer cells. Patients whose tumors have genetic changes that match one of the treatments in the trial may receive that treatment, if they meet other eligibility criteria. The trial seeks to determine whether treating cancer based on these specific genetic changes is effective, regardless of cancer type.

There are several treatment arms that are open to patients at any given time, each one enrolling patients whose tumors have a specific genetic change. Most treatment arms will enroll 35 patients. However, a few treatment arms address more common genetic changes, and for those up to 70 patients per arm will be enrolled. A few more treatment arms are expected to open in the future.

The drugs included in the trial have either been approved by the U.S. Food and Drug Administration (FDA) for another cancer or are still being tested in other clinical trials but have shown some effectiveness against tumors with a particular genetic change.

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FCI Finnish Cancer Institute

Syöpäjärjestöt

Hanketta tukemassa

AstraZeneca

Bristol-Myers Squibb

MSD

Pfizer

Roche

Takeda

YKSILÖLLISEN SYÖVÄNHOIDON MALLIMAA 2020