XV Encuentro de Cooperación Farma-Biotech

Novel orally available and selective CDK8 inhibitors

Madrid, 15 de noviembre de 2016

GOBIERNO DE ESPAÑA
MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD

MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

farmaindustria

Content

1. The Institution
2. The Product
   a) Target Indications
   b) Innovative mechanisms of action
   c) Differential features facing the market
   d) Current status of development
   e) IPR protection
   f) Pitfalls & Risks to be considered
3. Partnering Opportunities

CNIO: A comprehensive Cancer Research Centre

Experimental Therapeutics

The CNIO is a Comprehensive Center for Cancer Research with emphasis in translational approaches…

ETP-CNIO: Structure.

Experimental Therapeutics

Experimental Therapeutics

ETP-Biology

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Staff (7)

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J. Klett, Ph.D.
M.I. Albarrán, U.D.
M.C. R. de Miguel, Ph.D.
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E. Hernández, Ph.D.

"Plan Empleo Juvenil" (2)

A. Amezquita, V.E.T.
J. García, V.E.T

J. Pastor, Ph.D.

Key members with experience in Pharma industry (+ 10 years) and academic DD (+ 8 years)

Graduate Students (1)

F.J. García

Unit shared with SBBP: Crystallography and Protein Engineering (I. Muñoz / J.L. Martínez)

ETP-Medicinal Chemistry

S. Martínez, Ph.D.

Staff (7)

A.B. García, Ph.D.
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E. González, Ph.D.
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C. Varela, Ph.D.

"Plan de Empleo Juvenil" (3)

C. Fernández, U.D.
I. Arribas, U.D.
S. Sanz, V.E.T.

ETP-CNIO: “Bridging the Valley of Death in DD”

Experimental Therapeutics

CNIO

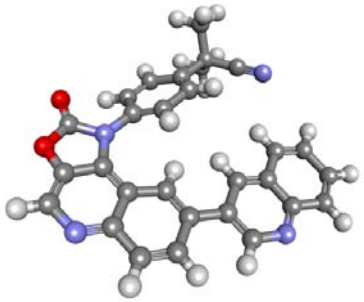
INNOVATIVE TARGETS THERAPY HYPOTHESES

PATIENTS BENEFIT

INNOVATIVE CANCER THERAPY

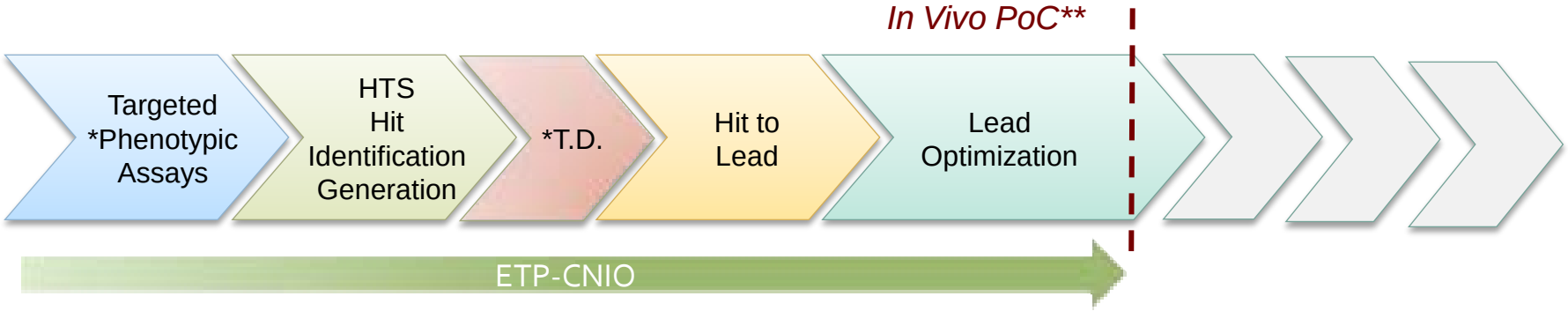
CNIO-ETP LEADS CANDIDATES PoC

PHARMA BIOTECH CLINICAL CANDIDATES



ETP-CNIO: ACTIVITIES

Experimental Therapeutics



*"Early" Drug Discovery Phases / In vivo PoC***

* T.D. Target Deconvolution

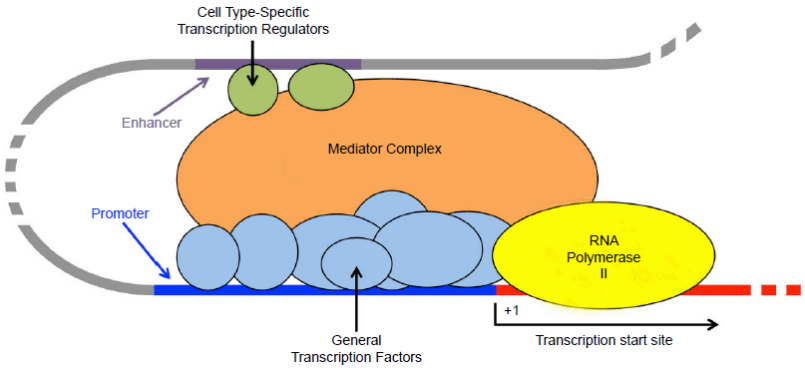
** PoC is achieved when an advanced lead compound is able to produce target associated biomarker modulation (PK-PD) and antitumoral efficacy in in vivo models of disease, after a preferred PO route of administration.

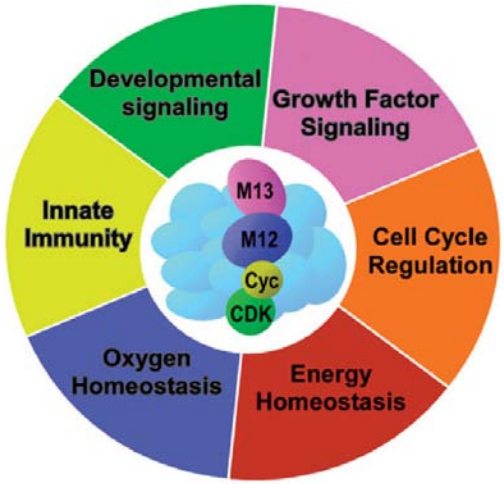
CDK8 Biology.

Experimental Therapeutics

- Cyclin-dependent kinase 8 (CDK8) is a serine–threonine protein kinase localized to the nucleus. CDK8 /Cyclin C are components of multi-protein Mediator complex that regulates gene expression by interacting directly with the transcriptional machinery and regulating RNA-Pol II activity.
- The CDK19 paralog shows high homology to CDK8 and is consider an isoform of CDK8 that it is also coupled with Cyclin C and is an alternative component of the Mediator complex.
- CDK8 is ubiquitously expressed, CDK19 is only expressed in prostate, salivary gland, thymus and testis.
- CDK8 does not play a "*direct role*" in cell cycle progression in contrast to some other members of the CDK family (for example CDK1, CDK2 and CDK4/6),

Functions of Mediator Kinase Complex



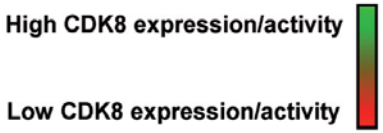


From Clark et al. Crit. Rev. Biochem. Mol.Biol. 2015; 50 (5): 393-426

CDK8 Biology.

Experimental Therapeutics

Mediator Oncogenic
Colorectal Cancer
Gastric Carcinoma
Melanoma
Prostate Cancer
Pancreatic Cancer
Ovarian Cancer
Breast Cancer
AML (leukemia)
Poor Survival outcome



Mediator (Tumor Suppressor)
Osteosarcoma
T-ALL (leukemia)
Endometrial Cancer
Uterine Leiomyoma

Adapted from Clark et al.
Crit. Rev. Biochem. Mol.Biol. 2015; 50 (5): 393-426

Mediator Kinase Complex as an oncogenic unit.

Known Mediator Kinase substrates / Oncogenic Mechanisms
(therapeutic setting reported)

p-E2F1 -> (+) Wnt/β-catenin signaling
Colorectal cancer

CCT251545, a CDK8/CKD19 inhibitor alters Wnt-β-catenin pathway regulated gene expression and has in vivo activity in WNT-dependent tumors (Colo-205 and SW620).
Nat Chem Biol. 2015. 12:973.
Other related compounds produce similar effects in same models.

Super-Enhancers associated gene transcription
(-) tumor suppressors genes
AML cell context dependent

Cortistatin A, a CDK8 inhibitor, upregulates SE-associated genes with tumor suppressor and lineage-controlling functions.
This effect is cell context dependent.
CA showed efficacy against AML xenografts after IP injection.
Nature 2015.526: 273-6.

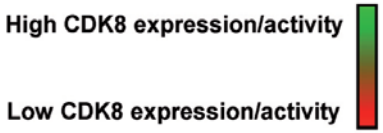
CDK19 is overexpressed in the progression of prostate cancer (PCa) and was associated aggressiveness and decreased survival.

Senexin A, *a CDK19/CDK8 inhibitor* led to significantly decreased migration and invasion of PCa cells *in vitro*.
J. Clin. Cancer Res. 2016 Sep 27.

CDK8 Biology.

Experimental Therapeutics

Mediator Oncogenic
Colorectal Cancer
Gastric Carcinoma
Melanoma
Prostate Cancer
Pancreatic Cancer
Ovarian Cancer
Breast Cancer
AML (leukemia)
Poor Survival outcome



Mediator (Tumor Suppressor)
Osteosarcoma
T-ALL (leukemia)
Endometrial Cancer
Uterine Leiomyoma

Adapted from Clark et al.
Crit. Rev. Biochem. Mol.Biol. 2015; 50 (5): 393-426

Mediator Kinase Complex as an oncogenic unit.

Known Mediator Kinase substrates / Oncogenic Mechanisms
(with therapeutic setting reported)

p-p27 -> (+) G2/M progression (proliferation).
Breast cancer with Skp2 and CDK8 expression.

(not reported)

(+) Tumor de-differentiation and ES pluripotency. *Colon tumors.*

Acute CDK8 loss in vivo strongly inhibited tumor growth and promoted differentiation. CDK8 depletion caused embryonic stem cells to differentiate.
Cancer Res. 2012 Apr 15;72(8):2129-39.

(+) Cooperation with oncogenic K-Ras. *Pancreatic cancer.*

Knockdown of either CDK8 or mutated K-ras contributed to attenuated pancreatic cancer growth in BALB/c nude mice.
Cancer Letters 356 (2015) 613–627.

p-STAT1S727 -> NK cells inactivation

CDK8 depletion or mutation of a single phosphorylation site (STAT1-S727A) enhances NK cell cytotoxicity against a range of target tumor cells. STAT1-S727A mice display significantly delayed disease onset in NK cell-surveilled tumor models including melanoma, leukemia, and metastasizing breast cancer.
Cell Rep. 2013 Aug 15;4(3):437-44.

CDK8 inhibitors (publications): Type I binding.

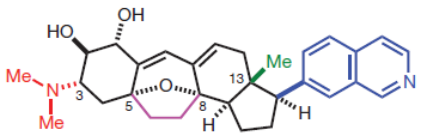
Experimental Therapeutics

Corstitatin A, a CDK8 inhibitor has anti-leukemic activity in vitro and in vivo through the inhibition of CKD8 and CDK19.

Cortistatin A upregulates SE-associated genes with tumor suppressor and lineage-controlling functions. This effect is cell context dependent.

CA showed efficacy against AML xenografts after IP injection.

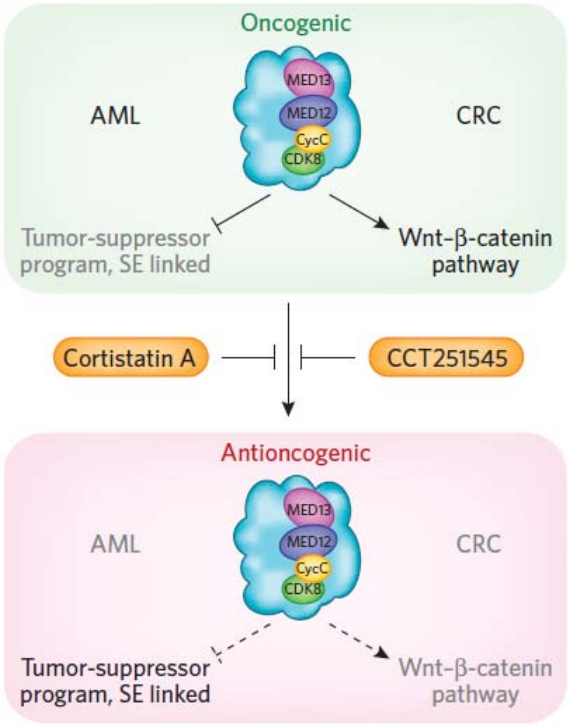
Pelish HE et al. Nature 2015.526: 273-6.



Preclinical Cortistatin A

Harvard

In vivo PoC studies with CDK8 inhibitors



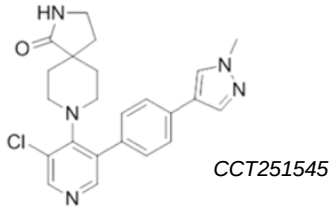
From T.G Boyer. Nat. Chemical biology 2016.

CCT251545 is a CDK8/CKD19 inhibitor that alters Wnt-β-catenin pathway regulated gene expression and other on target effects, including expression of genes regulated by STAT1.

CCT251545 has in vivo activity in WNT-dependent tumors (Colo-205 and SW620).

Dale T et al. Nat Chem Biol. 2015. 12:973.

CCT251545 Wnt activity SAR and SPR. In vivo PK-PD and efficacy in Colo-205 xenograft. Mallinger et al. J. Med. Chem. 2015, 58, 1717.



CCT251545

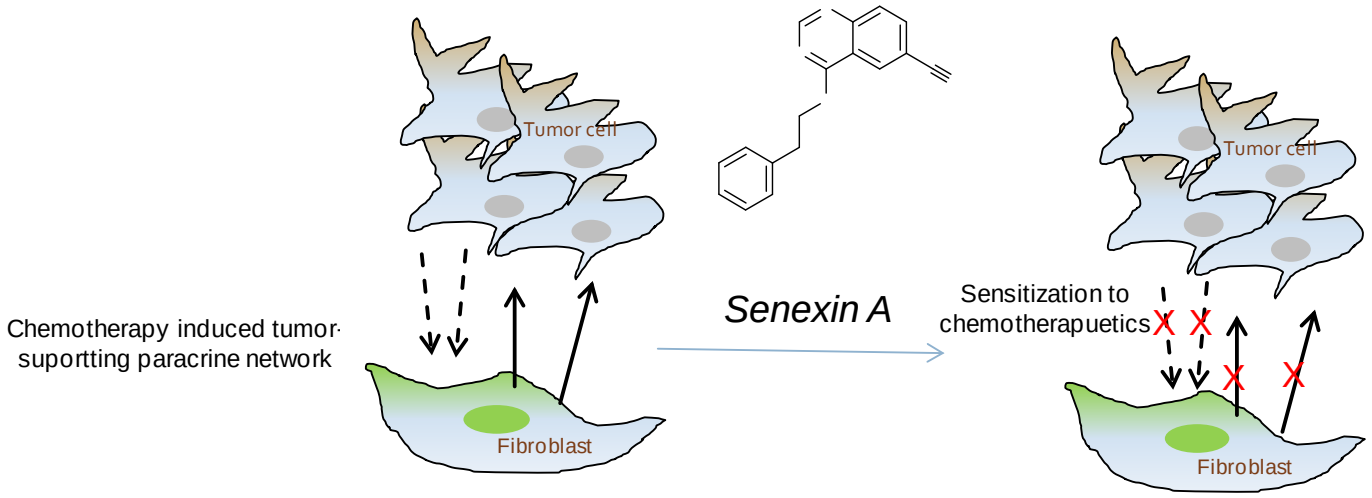
CRUK / Merck Serono

CDK8 inhibitors (publications): Type I binding.

Experimental Therapeutics

- Chemotherapeutics (Dox) induce tumor-promoting paracrine activities between tumor cells and normal fibroblasts. It has been proven that CDK8 inhibitor, Senexin A, suppresses them.
- Senexin A reverses the increase in tumor engraftment of A549 cells in tumor free mice pretreated with Doxorubicin.
- The inhibitor also increases the efficacy of chemotherapy (Dox) against xenografts formed by tumor cell/fibroblast mixtures.

Porter CD et al. Proc Natl Acad Sci U S A. 2012. 109(34):13799-804.



ETP-CNIO CDK8 inhibitors Summary.

Experimental Therapeutics

Target IV Assay Development | HTS HIT IV HIT Generation | HIT to LEAD Exploration | LEAD Optimization | Tech-Transfer Partnering

In vivo PoC

CNIO currently in development

LO / Available

CDK-8 inhibitors / CNIO

o A CDK8 inhibitor will be a **"First in Class" therapy** to treat cancer **including immunotherapeutic potential.**

o Screening platform up and running. Biochemical and functional cell based assays.

o Low-nM / picomolar highly selective CDK8-is (specific and combined with Target X inhibition).
o ETP-CDK8-is are cell active in the nM range in functional assays.
o Chemical series with SAR/SPR (ca. 100 analogues). X-ray information -> Type I binding mode.

o Anti-proliferative data in +40 cell lines: Identification of sensitivity achieved.
o ETP-CDK8-is show inhibition in "colony formation assays".
o Combination studies with selected ETP-CDK8-is. Synergistic anti-tumoral agents identified.

o ETP-CDK8-is are orally bioavailable.
o PK-PD study with our first lead CDK8-i ETP-827 shows preliminary positive results.
o ETP-827 *In vivo* Efficacy short term study in MOLM-13 xenografts with signs of efficacy.

o Chemical series protected with a patent application (PCT/GB2016).

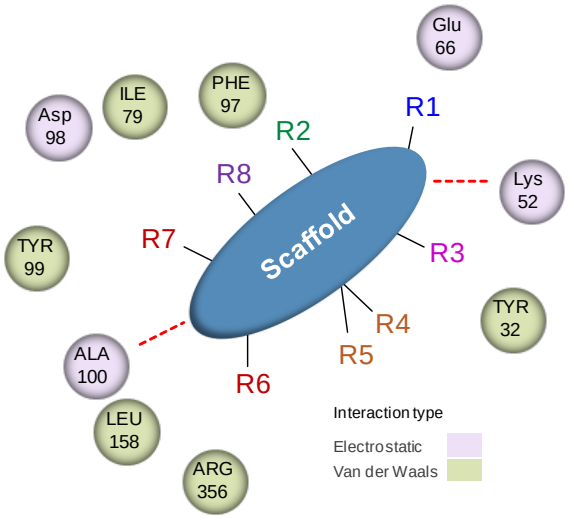
Current and future activities

o Full characterization of already identified (potential) improved leads . LO fine tuning of in vivo exposure.

ETP-CNIO CDK8 inhibitors Chemical Series

Experimental Therapeutics

- ETP-CDK8-is series bears a novel scaffold with 8 derivatizable positions for SAR/SPR exploration.
- Co-crystallisation of ETP-CDK8 inhibitors with CDK8/Cyc-C shows a Type I Binding Mode for these inhibitors with interactions with Ala-100 and Lys-52. (Type II inhibitors are poorly active in cells)
- Excellent Lead / Drug-likeness of ETP-CDK8-is chemical series. (MW / LogD / PSA / LEI / RoF).
- Selected examples of ETP-CDK8-is with IC_{50} (Biochemical) < 5.0 nM:
- EC_{50} p-STAT1: < 30 nM. // Soluble and permeable (> 100 μM / > 10^{-6} cm*seg^{-1}). // Microsomal stability. variable SPR. h-ERG binding > 30 μM. // No significant CYP-450 inhibition.



SAR / SPR
Multifactorial optimisation / Analysis

ETP-827 as a first lead for *in vivo* PoC studies

ETP-193 as an improved lead for in vivo PoC studies

Current LO activities focus: Fine tuning of in vivo exposure

ETP-CNIO CDK8-is Leads: ETP-827

Experimental Therapeutics

ETP-Number	CDK8 _IC50 (nM)	CDK19 _IC50 (nM)	STAT1-P(SER727) SW620 cell line EC50 (nM)	CDK1 _IC50 (nM)	CDK2 _IC50 (nM)	CDK4 _IC50 (nM)	CDK5 _IC50 (nM)	CDK6 _IC50 (nM)	CDK7 _IC50 (nM)	CDK9_IC50 (nM)
ETP-827	0,49	0,7	0,3	936	1020	10000	721	3690	3280	45.10

Selectivity ratio CDKs / CDK8: CDK1: 1912; CDK2: 2081; CDK4: 20408; CDK5: 1471; CDK6: 7530; CDK7: 6693; *CDK9: 92

* CDK9 cell activity (P-RNAPol-II) EC_{50}=2.37µM . Selectivity ratio cell activity CDK9/CDK8: 7900

Solubility Buffer_pH 7,4 (µM)	PAMPA_Papp (10^{-6} cm/seg)	h-LM_30 min. % Remaining	m-LM_30 min. % Remaining	r-LM_30 min. % Remaining	P450-1A2_% Inhibition @ 5,0 µM	P450-2C19_% Inhibition @ 5,0 µM	P450-2C9_% Inhibition @ 5,0 µM	P450-2D6_% Inhibition @ 5,0 µM	P450-3A4_% Inhibition @ 5,0 µM	HERG_Binding IC50 (µM)
> 100	13,26	100	29	83	< 5,0	< 5,0	24,1	< 5,0	34,2	> 30

KinomeScan™

468 Kinases tested @ 1.0 µM
Highly selective
S(35)= 0.06 y S(10)= 0.01

In Vivo PK (BALB-C Mice)

IV Clearance < 30% Hepatic Blood Flow
T 1/2 : 0.3 h (IV) / 0.4 h (PO)
Vd: 0.72 L/Kg
F > 90%

Plasma Protein Binding (% bound):
Mouse 57.8 / Human 89.9

Main off-target (potential duality). It seems a positive differentiating factor vs. competitors Opportunity

ETP-Number	Target X_IC50 (nM)	Target X activity SW620 cell line EC50 (nM)
ETP-827	20,60	9,86

Side by side comparison in antiproliferation and colony formation assays demonstrated superiority for ETP-827 vs. Senexin B and CCT251545 (no Target X inhibitors / Internal data)

ETP-CNIO CDK8-is Leads: ETP-193

Experimental Therapeutics

ETP-Number	CDK8 Biochemical_ IC50 (nM)	CDK19 _IC50 (nM)	STAT1-P(SER727) SW620 cell line EC50 (nM)	CDK1 _IC50 (nM)	CDK2 _IC50 (nM)	CDK4 _IC50 (nM)	CDK5 _IC50 (nM)	CDK6 _IC50 (nM)	CDK7 _IC50 (nM)	CDK9_IC50 (nM)
ETP-193	< 3,0	< 3,0	0,4	567	1500	N/T	> 200	10000	4020	> 100

Selectivity ratio CDKs / CDK8: CDK1: 259; CDK2: 685; CDK4: N/T; CDK5: 102; CDK6: 4566; CDK7: 1835; *CDK9: >50

* CDK9 cell activity (P-RNAPol-II) EC_{50} expected to be > 2.37µM . Selectivity ratio cell activity CDK9/CDK8: > 5000

Solubility Buffer_pH 7,4 (µM)	PAMPA_Papp (10^{-6} cm/seg)	h-LM_30 min. % Remaining	m-LM_30 min. % Remaining	r-LM_30 min. % Remaining	P450-1A2_% Inhibition @ 5,0 µM	P450-2C19_% Inhibition @ 5,0 µM	P450-2C9_% Inhibition @ 5,0 µM	P450-2D6_% Inhibition @ 5,0 µM	P450-3A4_% Inhibition @ 5,0 µM	HERG_Binding IC50 (µM)
N/T	N/T	100	95	90	N/T	N/T	N/T	N/T	N/T	> 30

KinomeScan™
N/T

In Vivo PK (BALB-C Mice)

Improved PK vs ETP-827
IV Clearance < 20% Hepatic Blood Flow
T 1/2 : 0.6 h (IV) / 0.9 h (PO)
Vd: 0.78 L/Kg
F > 90%

Plasma Protein Binding (% bound)
N/T

Main off-target (potential duality). It seems a positive differentiating factor vs. competitors Opportunity

ETP-Number	Target X_IC50 (nM)	Target X activity SW620 cell line EC50 (nM)
ETP-193	23,70	4,10

Side by side comparison in antiproliferation and colony formation assays demonstrated superiority for ETP-827 vs. Senexin B and CCT251545 (no Target X inhibitors / Internal data)

Currently ETP-193 is being profiled as a potential advanced lead vs. ETP-827. Additional ETP-CDK8-is selected for full characterization.

Reference CDK8-is: CCT251545 and Senexin B

Experimental Therapeutics

Internally generated data

ETP-Number	CDK8 _IC50 (nM)	CDK19 _IC50 (nM)	STAT1-P(SER727) SW620 cell line EC50 (nM)	Target X_IC50 (nM)	Target X activity SW620 cell line EC50 (nM)
ETP-827	0,49	0,7	0,2 / < 0,064 *	20,60	9,86
ETP-193	< 3,0	< 3,0	0,4 / N/T *	23,70	4,10
Senexin B	19,30	41,6	27,4 / 83 *	> 10000	N/A
CCT251545	1,60	1,4	4,9 / < 0,24 *	> 10000	N/A

Assay under IFN g stimulus. ETP-827 activity under these conditions < 0,064 nM.
N/A: not active at maximum concentration tested (10 μM). N/T: not tested.

ETP-827 and ETP-193 are more potent CDK8-is in cells than Senexin B and CCT251545.
Senexin B and CCT251545 are not Target X-is.

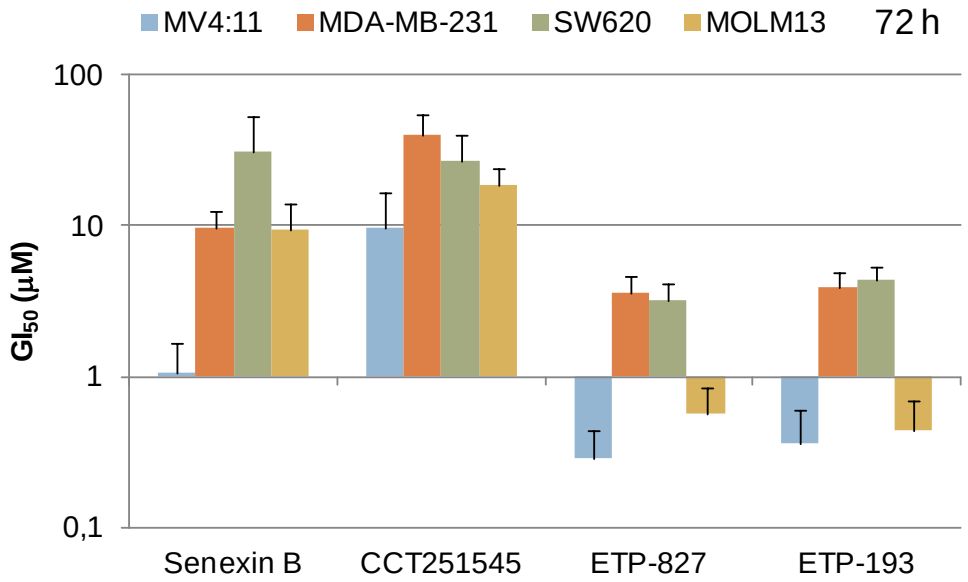
o Anti-proliferative data in +40 cell lines with ETP-827: most sensitive cell lines are AML.

o ETP-827 and ETP-193 are between 3x and 20x more potent than Senexin B and CCT251545 in proliferation assays for selected cell lines such as MV4:11, MOLM13, MDAMB231 and SW620.

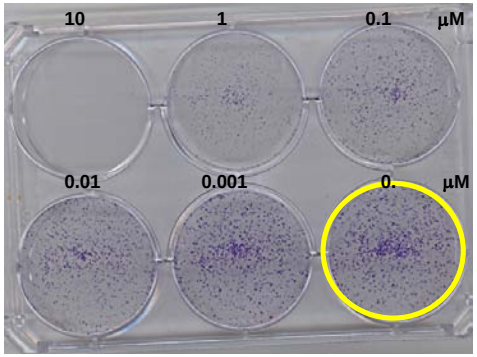
o ETP-827 Inhibition in colony formation assays is 8x more potent than Senexin B and CCT251545.

Antiproliferation and Colony Formation profiles.

Experimental Therapeutics

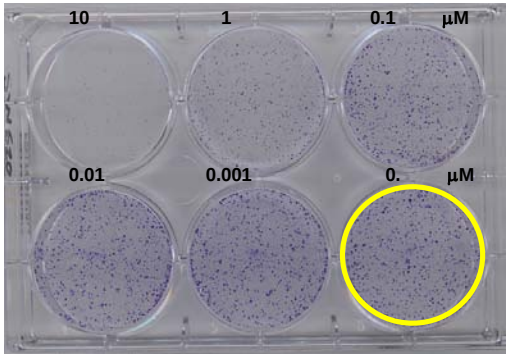


ETP-827



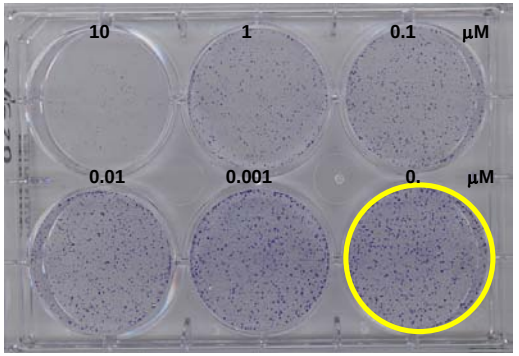
EC_{50} = 130 nM

Senexin B



EC_{50} = 940 nM

CCT251545



EC_{50} =1050 nM

CDK8 and Target X duality.

Experimental Therapeutics

Experimental combination of CDK8 and Target X inhibitors

ETP-Number	CDK8 _IC50 (nM)	STAT1-P(SER727) SW620 cell line EC50 (nM)	Target X_IC50 (nM)	Target X activity SW620 cell line EC50 (nM)	CHEMICAL PROBE
ETP-827	0,49	0,2 / < 0,064 *	20,60	9,86	DUAL
CCT251545	1,60	4,9 / < 0,24 *	> 10000	N/A	CDK8-i
ETP-914	412,00	2100,00	57,10	290,00	Target X-i

** Assay under IFN g stimulus. ETP-827 activity under these conditions < 0,064 nM. N/A: not active at 10 μM.*

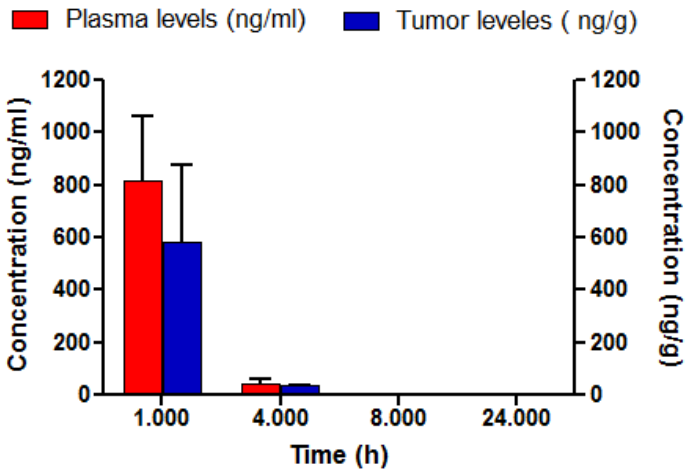
Combination of CCT251545 + ETP-914
Antiproliferation and colony formation assays.

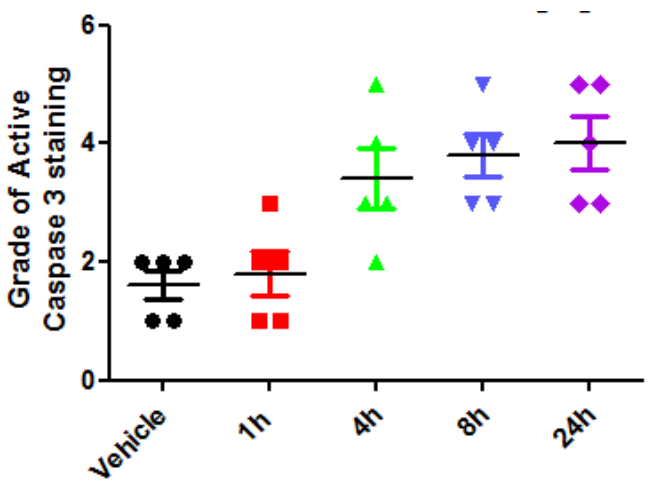
CDK8 and Target X inhibitions are synergistic and produce a comparable outcome to dual ETP-827 profile.

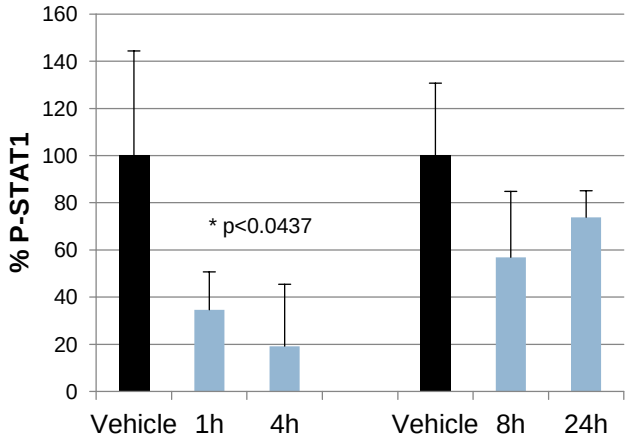
First Lead ETP-827: PK-PD vs p-STAT1.

Experimental Therapeutics

PK/PD study wih ETP-827@ 5mg/kg in SW620 xenograft







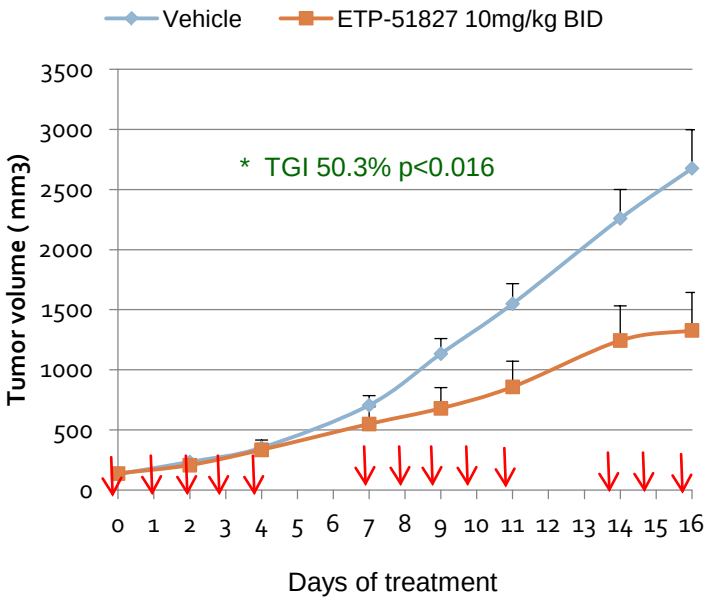
ETP-827 distributed well between plasma and tumor with a short half life (as expected from PK data).
It modulates p-STAT-1 up to 4h.
It is expected that ETP-193 with longer T1/2 and higher Vd will improved this results.

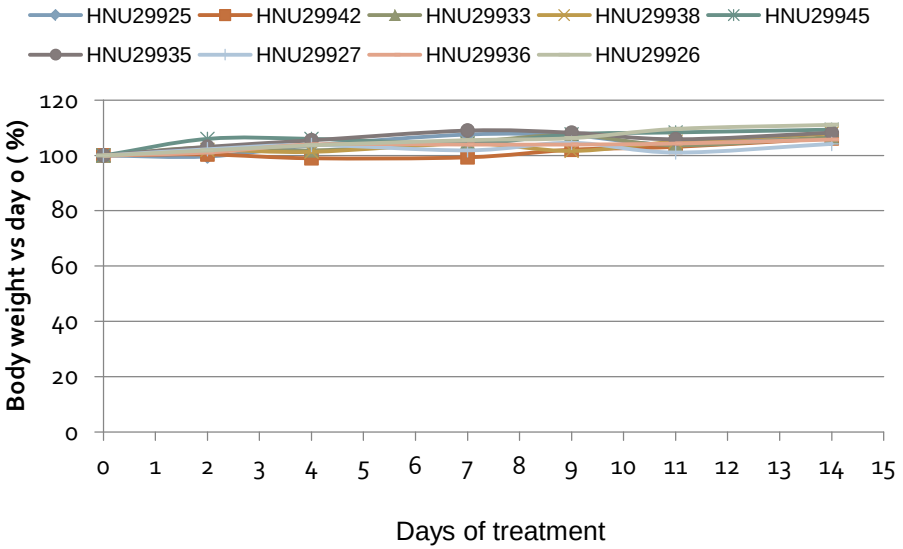
ETP-827 produced a sustained apoptotic effect for 24 h, at time points where compound is not detected in tumor.

First Lead ETP-827: Efficacy in MOLM13 xenograft.

Experimental Therapeutics

Treatment with ETP-827 @ 10 mg/kg BID in MOLM-13 xenograft





Treatment showed efficacy in a short term study.

Treatment is well tolerated with no body weight losses.

Immuno-deficient mice

CDK8 and NK cells.

Experimental Therapeutics

- CDK8 has been identified as a major kinase for STAT1-S727 phosphorylation in response to IFN signaling.
  Bancerek et al. Immunity. 2013 Feb 21;38(2):250-62.
- STAT1-S727 phosphorylation has an inhibitory role for NK cell cytotoxicity. Mutation of a single phosphorylation site (STAT1-S727A) enhances NK cell cytotoxicity against a range of target tumor cells.
- STAT1-S727A mice display significantly delayed disease onset into lungs after IV injection of melanoma B16F10 cells and orthotopic transplants of 4T1 breast cancer cells (metastasizing breast cancer).

  Putz et al. Cell Rep. 2013 Aug 15;4(3):437-44.

AUTHOR'S VIEW
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STAT1-S727 - the license to kill

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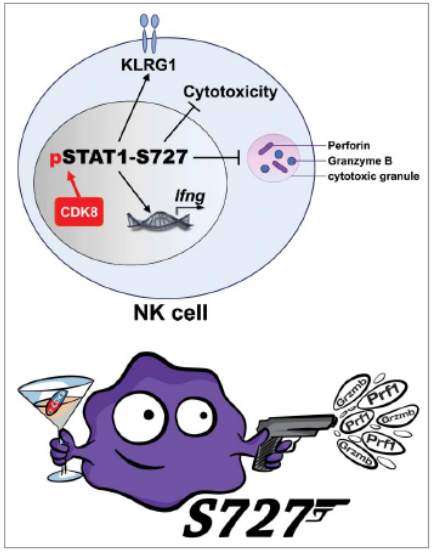
Keywords: CDK8, immunotherapy, NK cells, STAT1, tumor immune surveillance



There is a great demand for pharmaceuticals that can effect both tumor cell destruction and immune cell activation.

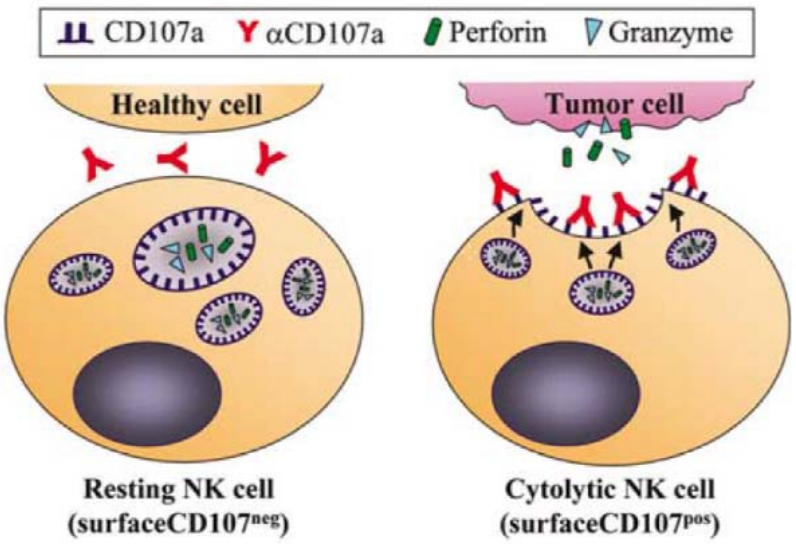
Taken together, CDK8 inhibitors may effectively kill 2 birds with one stone, attenuating bulk tumor cells while licensing NK cells to target cancer (stem) cells.

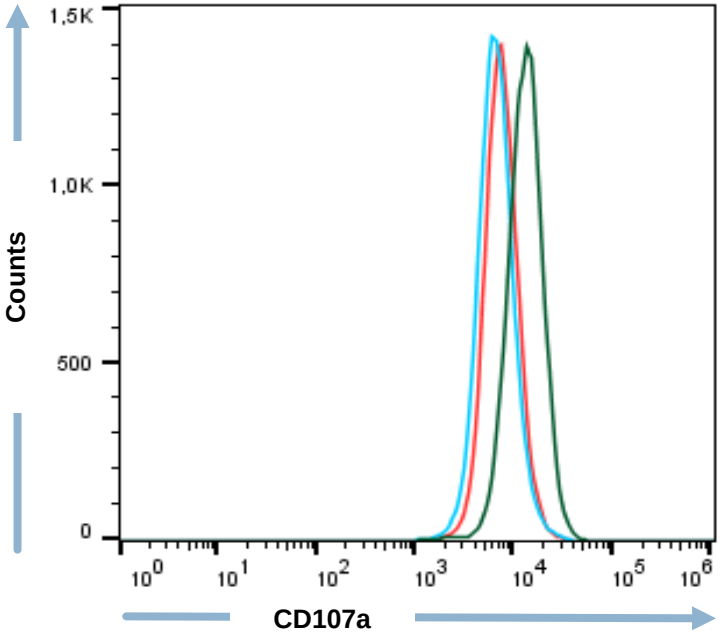
In leukemia, there is evidence that NK cells are able to eradicate leukemic stem cells and control minimal residual disease.

ETP-827 increases cytotoxicity of NK cells?

Experimental Therapeutics

ETP-827 enhances NK-cells degranulation





Buffer only / +DMSO / + ETP-827 dissolved in DMSO

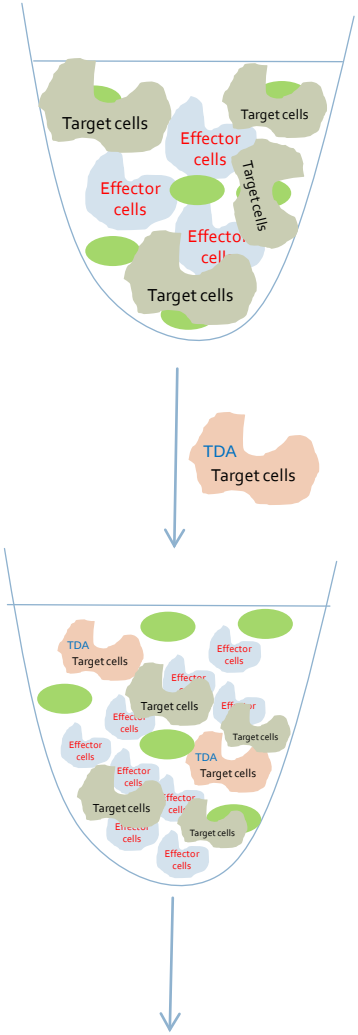
Expression of CD107a as read-out for degranulating NK cells

Treatment of NK-cells for 18h with ETP-827 @10μM induces expression of CD107a in the membrane.

In collaboration with H12O-CNIO Haematological Malignancies Clinical Research Unit

ETP-827 increases cytotoxicity of NK cells ?

Experimental Therapeutics



III. Measurement of NK mediated cytotoxicity after 4h by the detection of TDA in the medium

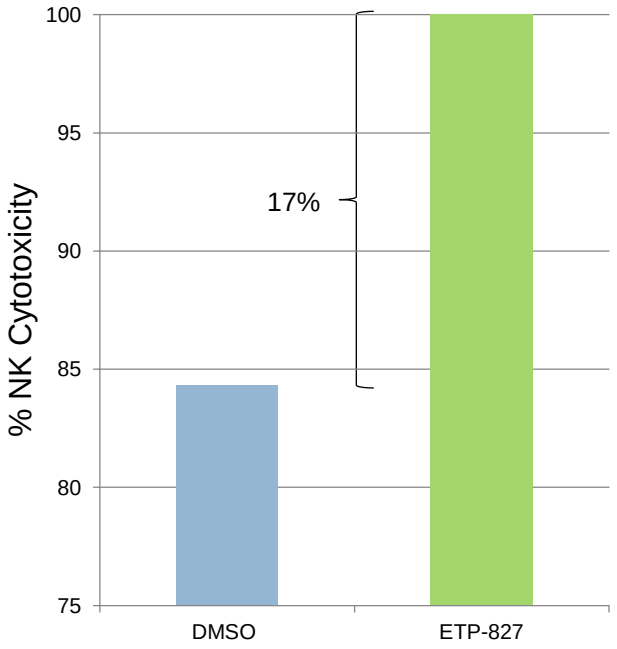
NK cytotoxicity assay

I. 18h Treatment of co-cultured NK-92MI and K562 (10:1) with DMSO or ETP-827 @10μM

ETP-827

II. Addition of Labeled target cells (K562) in a ratio E:T = 20:1

Preliminary Results



Treatment of co-cultured NK / Target cells with ETP-827 for 18h significantly increases NK cells cytoxicity against TDA-K562 target cells.

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Potential Risks / Pitfalls

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CDK8-inhibition in healthy non-targeted tissues?

- There are tumors where decrease expression/activity of the Mediator has been established, therefore suggesting a tumor suppressor role for it (CDK8) and conversely a potential tumor promoter role for CDK8-inhibitors in such tissues / compartments (i.e. T-ALL).

- It is not likely that CDK8 inhibition in those "healthy" tissues will be sufficient to induce tumorigenesis in the absence of other oncogenic events.

Example:

- The loss of mediator activity (haploinsufficiency of Cyc-C) collaborates with pre-established elevated levels of ICN1 to accelerate the development of T-ALL in mice.

- Cyc-C loss is able to increase ICN1 levels. However these levels on their own are not sufficient to expontaneously develop T-ALL. Other oncogenic alterations (i.e. LMO1) are needed to accelerate tumorigenesis.

Predictive biomarker for clinical response.

- P-STAT1 (S727) can be use to measure cellular inhibition of CDK8 activity, but there is no correlation with sensitivity to *in vitro* proliferation inhibition. (i.e. Cortistatin A study).

- Best to check expression of CDK8 and other mediator components and interactive genes.

Partnering Opportunities

Experimental Therapeutics

We offer to you:

- o A series of highly potent ETP-CDK8-is with highly desirable Lead-Drug-like properties.
- o I.P. protected series with high potential to deliver a clinical candidate after fine optimization.
- o Specific CDK8 and dual activity CDK8- Target X profiles (as a positive differentiating factor).
- o First lead ETP-827 has served to achieve preliminary in vivo PoC studies.
- o Improved PK lead ETP-193 identified which could be a candidate for development.
- o Other potential leads already in the pipeline.
- o Project platform up and running and experience in the field of CDK8 inhibition.
- o Structural information generated for CDK8 and Target X.
- o Back-up series identified.

"CDK8-is can serve to treat "bulk tumor cells" + activate immunotherapy response + treat metastasis + make chemotherapeutics drugs more efficient + eliminate the tumor initiating capacity of cancer stem cells + cooperate with targeted drugs against prominent oncogenes in highly deadly cancers (i.e. Kras)"…

We are willing to partner our project under several scenarios:
Licensing / Project Co-development …

Thanks

Experimental Therapeutics

Experimental Therapeutics Programme. Current and past members.

Molecular Oncology Programme
Tumour Suppression (M. Serrano)
Telomeres and Telomerase (M.A. Blasco)
Cell Division and Cancer (M. Malumbres)
Genomic Instability (O. Fernández-Capetillo)
Brain Metastasis (M. Valiente)
Experimental Oncology (M. Barbacid)

Clinical Research Programme
Gastrointestinal Cancer Clinical Research Unit
H12O-CNIO Haematological Malignancies CRU

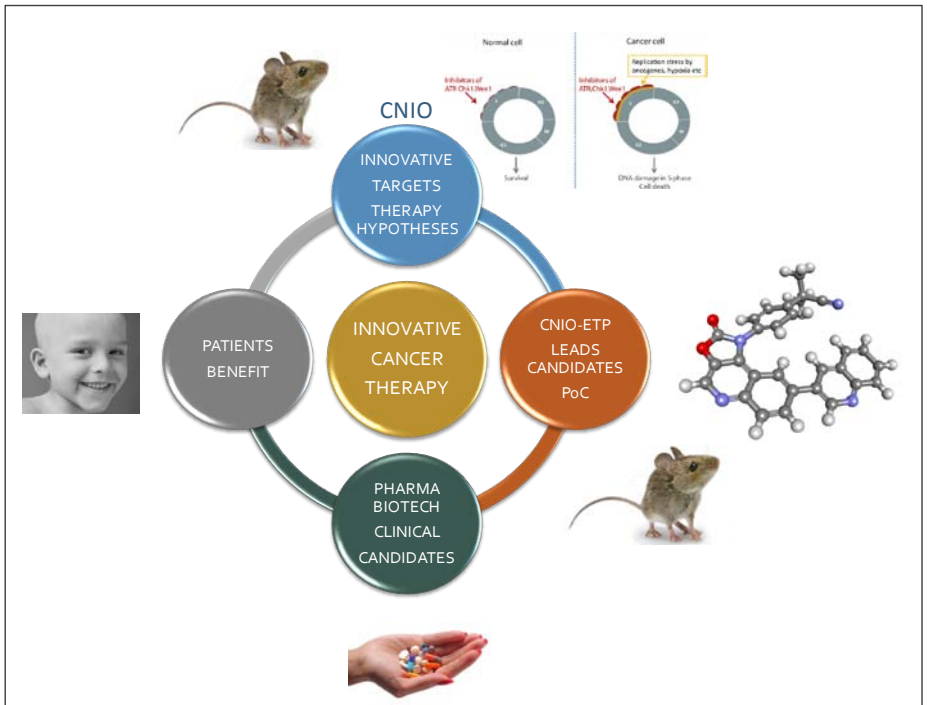
Structural Biology and Biocomputing Programme
Cell Signalling and Adhesion (D. Lietha)

Spectroscopy and Nuclear Magnetic Resonance Unit (R. Campos)

Biotechnology Programme Units

Technology Transfer and Valorisation Office
Communication Office

Crystallopgraphy and Protein Engineering Unit
(I. Muñoz / J.L. Martínez)



"Some ideas may just stay on paper forever, but others have a way forward to make it into a pill to help patients, perhaps our relatives, our friends, ourselves"

Centro Nacional de Investigaciones Oncológicas

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INFLECTION BIOSCIENCES