

The information system in a small biotech company: Overview of the cheminformatics developments at Aptanomics

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Contents

- Introduction
- Chemical library management
- HTS data management and analysis
- Lead development and pipeline snapshot
- Conclusion



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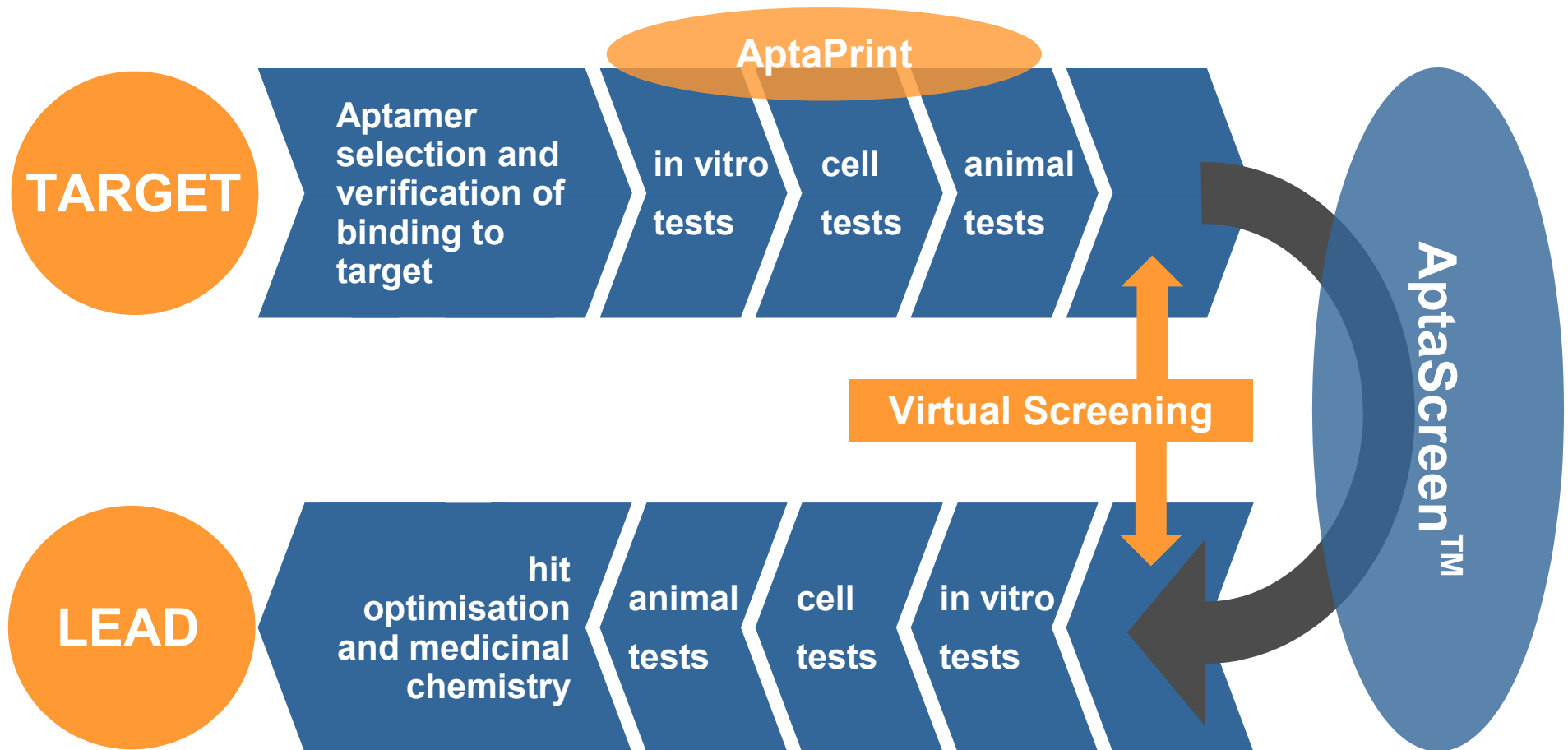


Aptanomics

- A small biotech company founded in 2001
- Discovers and develops new drugs
- Targets involved in deregulated signaling pathways, resulting in uncontrolled cell growth and survival
- Discovery engine based on peptide aptamers
- Identify new druggable sites by AptaPrint
- Drugs are identified by AptaScreenTM (HTS) or virtual screening
- Offers collaboration opportunities for small molecule discovery



Workflow





Cheminformatics

Requirements

- Chemical library management
- H.T.S. data management and analysis
- Hit to lead data management and analysis
- Reliable, flexible, upgradable and based on standard technologies



Cheminformatics

I.T. Resources

- L.A.M.P. application server, a storage server and a H.P.C.
- 1 I.T. developer and several users for evaluation
- In-house knowledge on standards and Open-Source software

R&D Resources

- Commercial software for library design and compound acquisition strategy (Tripos)
- Commercial computational chemistry and modeling platform for drug discovery programs (Molsoft LLC)



Cheminformatics developments at Aptanomics

Chemical library management

- Introduction
- **Chemical library management**
- HTS data management and analysis
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Overview

Features

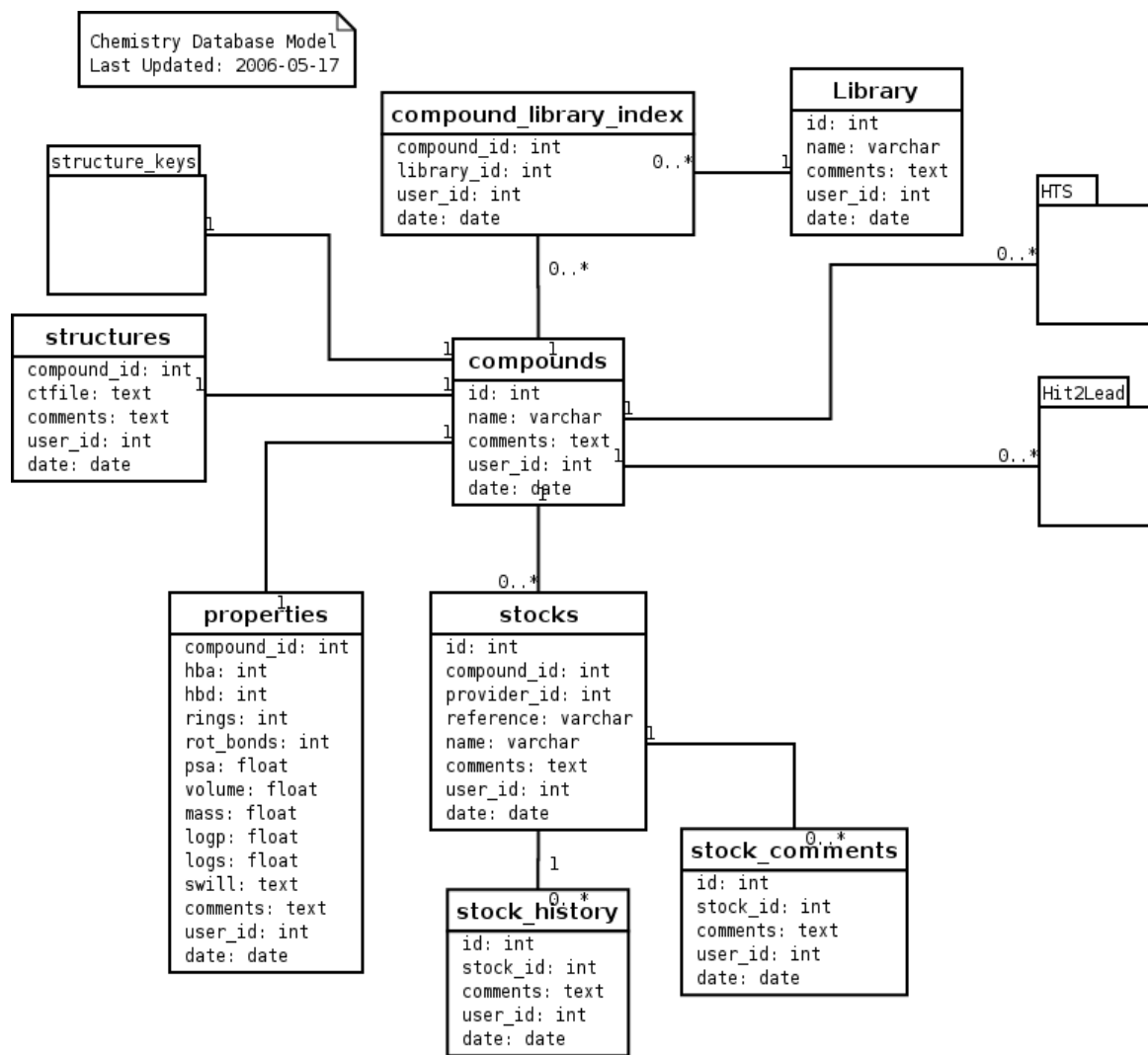
- Compound, library and stock management
- Web interface
- Molecular structures and descriptors
- Structure similarity searches against internal or commercial libraries

Solution based on

- PHP scripts for the User Interface and simple functions
- Jmol for dynamic structure visualisation (jmol.sourceforge.net)
- Python script for MySQL databases management
- ICM (Molsoft LLC) for molecular descriptor calculation



Database Design





Compound Datasheet Screenshot

AptaScreening

Aptanomics Screening Facilities

Calendar go

Screening | Molecules | Hit2Lead | Pipeline | Logout

Descriptions	Molecular Structure
APTA-ID APTA-000892	 Jmol
Common name Roscovitine (change)	
Libraries Cdc4 (change)	
Plate CDC-384-0003-00-01	
Well H02	
Molecular Weight 354.459	
LogP 3.06211	
Stocks Lot A : (Lot en plaque 384) Lot B : 0mg	
Comments + (change)	

Molecular Parameters :

HBD	HBA	Rings	Rot.	psa	Vol.	M.W.	LogP	LogS	Lipinski	Veber	Swill	Penalty
3	4	3	8	71.2249	343.224	354.459	3.06211	-5.39622	Yes	Yes		0
< 5	< 8	< 5	< 13	< 155	650>X>100	550>X>200	6.0>X>-2.5	0.5>X>-6.5	Yes	Yes	None	(range for 95% of drugs)

Screening:

- [Cdc4/c21Luc-Skp1/s8Ruc \(79.72748 / 23.32199 \)](#)



Cheminformatics developments at Aptanomics

H.T.S. data management

- Introduction
- Chemical library management
- HTS data management and analysis
- Lead development and pipeline snapshot
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Overview

Features

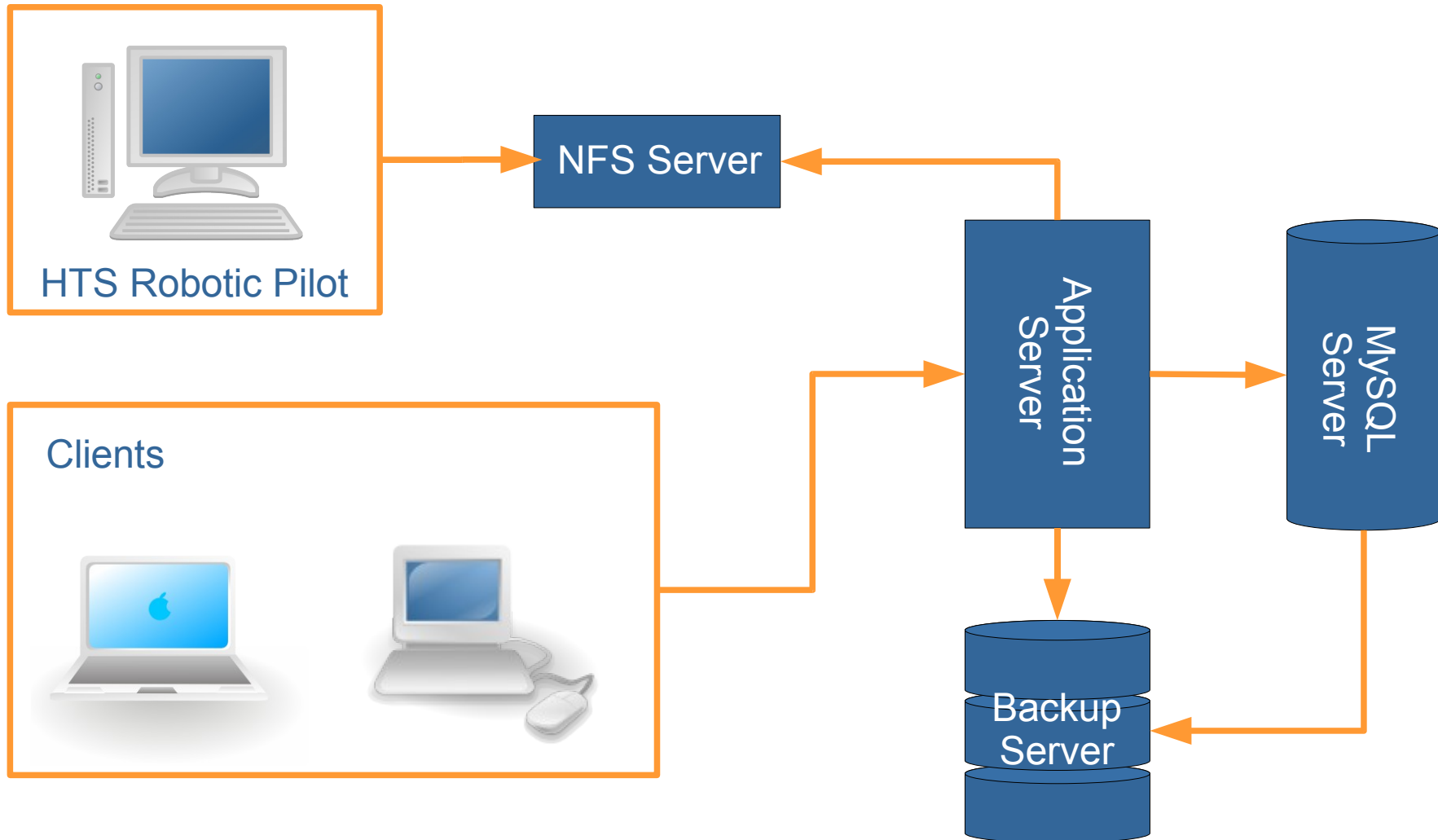
- Easy management of H.T.S. data (storage, retrieval, analysis)
- Automatic download of H.T.S. data from robotic platform
- Seamless interface with our compound management system
- Screening data mining

Solution based on

- Web interface and secure data management
- C++ software for data analysis
- MySQL User-Defined Functions for statistics
- Java applet for dynamic data visualisation



Multi-Tier Architecture





Cheminformatics developments at Aptanomics

H.T.S. data management

Plate Overview

Treated HTS Data

	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
A	-15.9	-8.1	-33.8	-24.3	-11.9	-33.8	-9.8	-3.0	-12.5	19.4	20.4	-14.2	12.7	-14.1	-28.7	-14.7	-24.7	47.9	-24.4	-8.6	-1.5	39.2	-30.1	73.3
B	20.1	-18.8	-17.3	15.8	2.2	-24.3	16.3	-12.7	-24.9	-36.4	6.9	64.1	-17.4	-4.9	-11.8	55.8	75.2	14.5	-14.3	-1.1	-27.6	-17.7	-21.3	109
C	71.7	14.5	40.5	14.3	6.8	8.2	9	10.9	-6.2	-4	13.4	-6.8	24.6	9.2	7.7	-5.9	6.9	25	-1	-7.2	12.8	9.6	-29.1	39.8
D	37.3	37.4	2.7	-1.6	11.5	33.1	4.3	14.3	4	-5.5	4.9	-4.5	12.5	-4.7	-0.4	5.3	-3.4	-1.8	20.1	9.4	4.6	63	-30.7	100.7
E	49.2	-13.6	-29.2	-11.8	-20.5	-15.7	35.6	11.9	-6.7	-20.7	6	6.9	23.1	-12.8	-17.7	-21.6	-7.8	23.3	-17.9	-12.8	-21.4	6.9	-67.9	33.3
F	34	30.8	25.3	38.5	35.8	17.8	1.4	6.5	75.9	-4.4	8.6	15.3	-1	31.8	-3.7	2	-5.4	8	38.2	15	-84.5	-10.3	-57.3	33.3
G	19.7	2.2	-17.9	-3	-13.8	-4.3	-4	-4.9	-14.3	4.3	21.3	-2.7	-1.1	2.4	-6.9	4.8	30.8	17.5	-14.9	16.6	55.6	-3.5	-31.2	100.3
H	13.1	-15.4	-5.9	-6.5	30.8	4.6	-2.2	-4.6	1.7	-20.5	-6.7	1.1	-0.6	-8.2	-10.9	-10.3	5.1	-69.7	-73.5	8.5	8.7	-6	-33	100.3
I	46.9	25.3	34.3	0.4	13	9.1	6	15.4	-5.8	5.2	33.3	15.9	3.9	11.9	35.7	13.3	38	11.1	33.4	13.2	9.9	0.1	-17.6	100.3
J	-5.6	6.5	12.7	4.6	2.9	4.9	10.5	4.3	17.1	5.9	24.6	14.4	68.3	10.5	24.6	11	17.9	14.8	20.9	13.4	36.1	33.5	-17.6	100.3
K	3.9	4	62.0	-5	26.1	-14.9	-10.7	-12.7	-1.2	-3.9	-11.7	-10	-13.9	-12.6	-23	-8.8	-17.1	-20.4	13	-19.4	-26.5	-12.5	-40.1	100.1
L	-14.9	-11.3	-7.5	4	77.4	-8.4	-4	-14.9	-9.7	11.5	-14.3	-20.3	-5.7	-8.2	-1.2	-9.1	-13.6	-6.7	-4.5	-24.2	-22.3	-15	-39.3	100.7
M	11	16	79.9	-0.2	11	20.6	6	9.7	6.5	6.8	13.3	15.5	24	3.4	16.6	37.3	2.2	12.4	43	22.4	9.5	45.8	-2.2	100.3
N	18.9	21.8	4.9	6.5	67.3	1	6.4	1.5	24.1	4	15.6	-22.8	9.2	56.2	24.2	16.9	7.4	9.8	10.9	24.8	5.7	8.2	1.2	33.3
O	-14	5.6	1.2	-15.8	27.2	-12.7	-9.8	-19.8	12.6	-11.4	-14.2	-17.3	-31.6	-14.5	-12.3	-18.3	-19.5	-14.7	-17.2	15.6	38.1	-12.5	-32.9	33.3
P	-20.5	-26.9	13.7	-21.5	14.8	-27.8	28.5	-4.6	62.2	-17.9	-21.3	15	-16.9	-25.7	-30.2	-13.9	-25.5	-23.4	-36	-21.8	-29.8	-24.6	-32.9	33.3

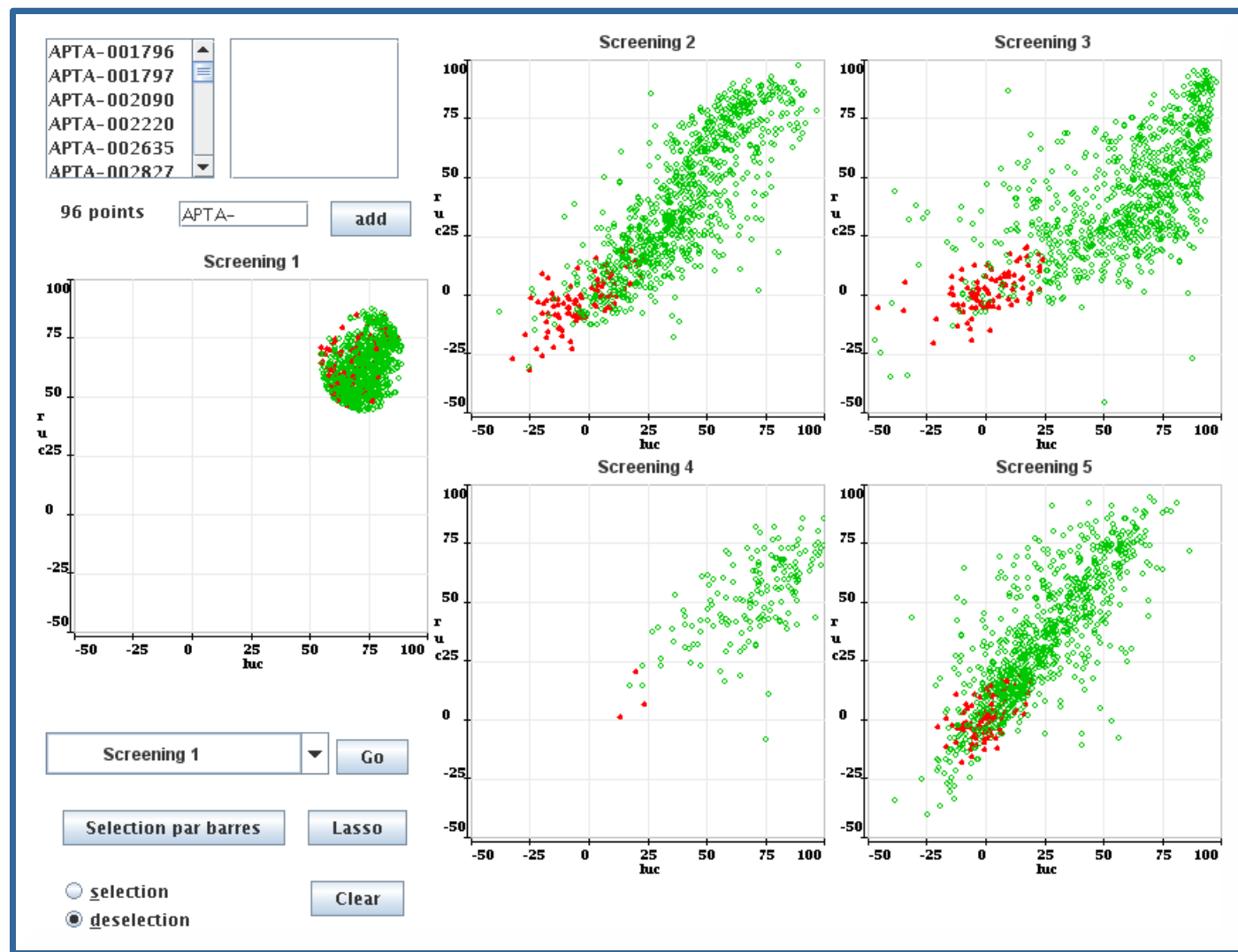
Raw HTS Data

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
A	141840	119680	137540	119140	107600	119400	100080	111820	100700	10380	71060	99720	78200	102680	115360	108260	113440	33420	124040	117440	113740	80320	180520	3500
B	97240	124580	117280	78260	89800	105520	73860	93340	106700	112980	79460	32120	99300	90360	97700	42400	14840	80900	107880	103340	131440	140980	152440	3480
C	31700	94260	57460	83720	84480	80020	79780	77360	85860	86700	71000	86500	82400	78060	78740	90140	82940	59600	99160	104280	101360	107120	140500	3640
D	80520	15840	78840	83130	67720	15080	72900	89720	73640	83460	74950	80800	67980	81780	81820	77500	85570	86880	79160	92420	108000	19540	131220	3260
E	48710	108320	98520	89380	90660	85860	49660	66460	77720	88860	88960	67580	56880	86300	91140	96020	88280	65640	106200	106680	133480	105620	158520	3480
F	86880	67900	58420	49920	47770	18440	67520	67730	19710	74860	64780	61700	73520	9600	79880	80400	90560	81640	50700	87150	202380	123100	150100	3940
G	80460	96020	87300	77880	80150	71680	71840	73910	78580	86150	55340	69960	69320	69520	77900	73140	57340	70740	105240	82780	30740	116360	127700	3360
H	85440	110360	81960	79200	48800	64620	88710	71960	66620	80420	70460	65940	65600	73620	76400	80340	74500	136460	150340	87280	93780	111120	126600	3940
I	52100	75460	15620	77540	63120	64960	84560	60680	74020	66000	15120	58560	66760	62680	46500	65100	51280	75000	17740	82200	91180	101700	116820	2920
J	103220	97380	74980	76980	72180	68320	63440	68700	59700	67880	54800	61540	14930	65000	55400	68820	68820	74140	73060	84760	68900	72340	121600	3150
K	104980	97740	33620	83420	55280	84360	79000	80060	72500	73880	79060	78960	79880	79180	87660	80860	86600	95500	74320	104920	121260	113560	141140	3320
L	125140	115540	97080	81400	10580	83220	76480	85720	80020	86840	83260	88100	77510	81920	76680	82040	88760	87770	91520	111340	121440	119360	143820	3320
M	93820	94340	72400	88980	74980	66260	73260	72500	74700	75860	70320	69080	63220	79260	70920	18120	86040	79540	54340	75300	95460	61120	114040	3080
N	88120	93060	97820	90980	50880	85480	76500	81660	61680	79820	71280	103960	78320	39540	68000	76680	87860	86880	88460	78440	107040	109220	116700	3820
O	141660	99760	99320	106320	67700	95980	95180	99020	75680	92840	96700	97160	110920	98340	98140	107660	106480	107300	110520	86860	95520	134880	166760	4040
P	147340	139960	89900	116460	36880	114160	86360	90680	36110	101420	106460	75110	103600	112720	116680	107520	114140	121900	135260	131260	144520	161020	184280	3680



Scatterplots

- Scatterplot visualization of HTS and physico-chemical data
- Dynamic interface
- Multiple-entry point graphical selections
- Selection A (e.g. ex biological filter) becomes source collection for Selection B (e.g. ex chemical filter): allows for multiple-step orthogonal filtering
- Rapid identification of relevant hit candidates and chemical series





Cheminformatics developments at Aptanomics

Lead development

- Introduction
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- **Lead development and pipeline snapshot**
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Overview

Features

- Structural, biochemical and cell assay data management
- Link with molecular properties
- Combined analysis of in silico, in vitro and in vivo assays

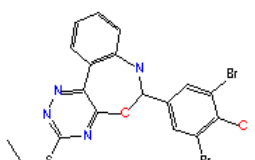
Solution based on

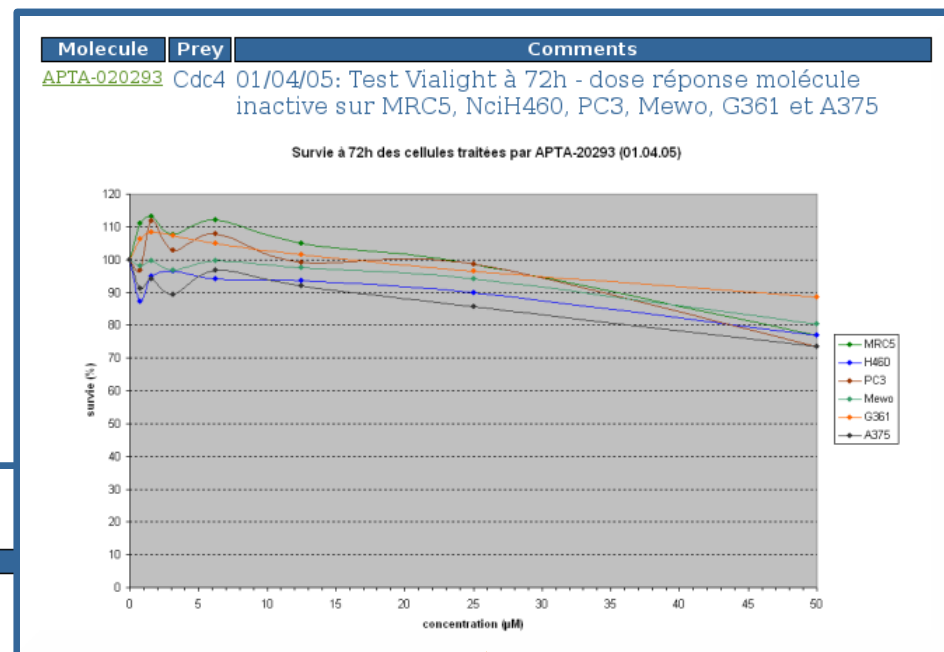
- PyMOL for batch generation of 2D molecular picture
(pymol.sourceforge.net)
- XML data file
- GD2 library (PHP) for dynamic image generation



Hit2lead Screenshots

Apta-ID	Interaction	Cells	Yeast	Biochem	Structure
APTA-020293	Cdc4 / c21	graphs			

✓	Serie	Structure
		



Apta-ID	Name	Interaction	Comments
APTA-020293	Aranocyl	Crc4 / c21	

Cell
01/04/05: Test Vialight à 72h - dose réponse
molécule inactive sur MRC5, NciH460, PC3, Mewo, G361 et A375

Yeast
Dose réponse du 01/04/05 (max. 50µM)
Effet plus marqué sur les souches Crc4 mais DR n'a pas l'aspect sygmoidal d'un produit inhibiteur comportement plus lié à une toxicité (dose max 50µM)

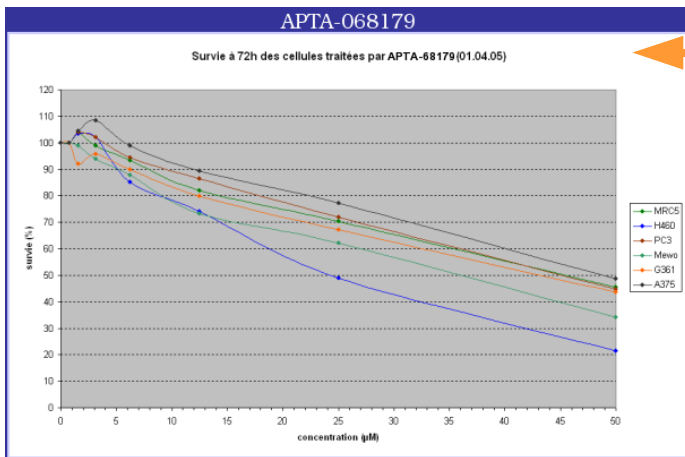
Biochemistry

Structure



Pipeline Screenshots

- Synthetic overview of pipeline advancement (chemical, biochemical, cellular data)
- One-click access to in depth data sheets
- Rapide mouseover visualization of critical lead development data (structures not shown here)





- Introduction
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Conclusion

- Cheminformatics solutions cover the entire Discovery activity spectrum
- Custom interface entirely developed in house
- I.T. solutions based on Open-Source software, with full compatibility with industry standards
- Reliable, upgradable and cross-platform system



Aptanomics Cheminformatics and Informatics

- Matthieu Schapira, Head of Chemistry and Cheminformatics
- Jérôme Pansanel, Scientific Information System Manager