The Mobile Kinome

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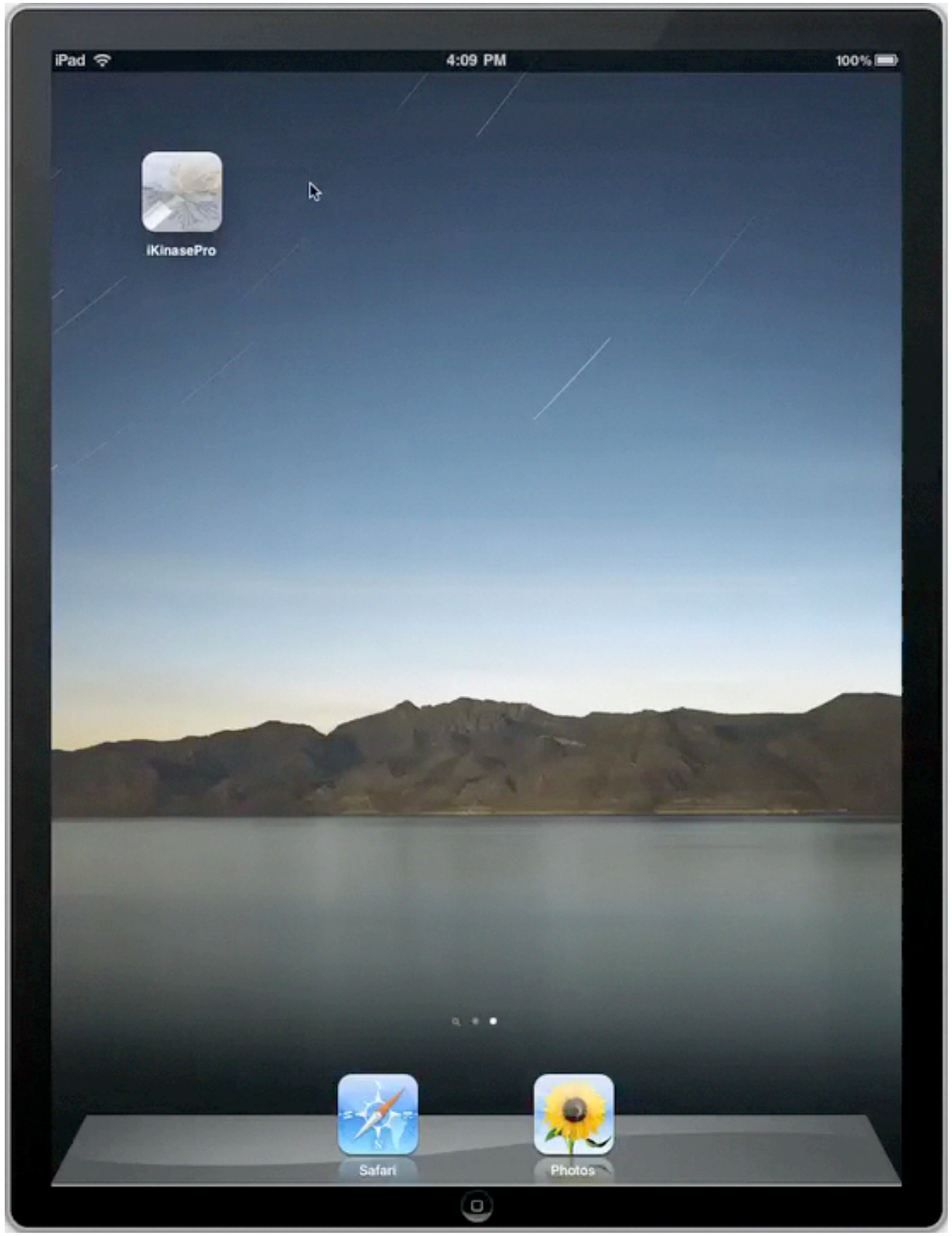
Presentation Agenda

- Demo
- Background
- Infrastructure
- Looking “Under the Hood”
- Application Availability

Starting with a Demo...



iKinasePro

An iPad App in the Cloud

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Background: Multi-Kinase Inhibitors

Nature Reviews | Drug Discovery Vol 8 | February, 2009

Table 1 | **Selected multi-target kinase inhibitors**

Drug (company)	Target	Highest phase	Indication*
Sorafenib (Bayer and Onyx)	PDGFR, VEGFR2 and 3, FLT3, KIT, RET, RAF	Launched	Hepatocellular carcinoma, RCC, renal tumour
Dasatinib (BMS)	BCR–ABL, FYN, SRC, LCK, EPH	Launched	ALL, CML
Nilotinib (Novartis)	PDGFR , ABL, KIT	Launched	CML
Sunitinib (Pfizer)	PDGFR, VEGF2, FLT3, KIT	Launched	Gastrointestinal tumour, RCC
Motesanib (Amgen and Takeda)	PDGFR, VEGFR, KIT	Phase III	NSCLC
Vandetanib (AstraZeneca)	EGFR, VEGFR2, RET	Phase III	Thyroid tumour, NSCLC
Lestaurtinib (Cephalon)	JAK2, FLT3, TRKA	Phase III	Myeloid leukaemia
XL184 (BMS and Exelixis)	VEGFR2, MET, KIT, FLT3, RET, TEK	Phase III	Thyroid tumour
Pazopanib (GSK)	PDGFR, VEGFR1, 2 and 3, KIT	Phase III	Renal tumour, sarcoma

*Indication given for highest phase; all drugs are also in lower phase clinical trials for other oncology indications. ALL, acute lymphoblastic leukaemia; BMS, Bristol–Myers Squibb; CML, chronic myeloid leukaemia; EGFR, epidermal growth factor receptor; GSK, GlaxoSmithKline; NSCLC, non-small-cell lung cancer; PDGFR, platelet-derived growth factor receptor; RCC, renal cell carcinoma; VEGFR, vascular endothelial growth factor receptor.

Imatinib (Gleevec: Novartis)	**ABL, PDGFR, KIT**	**CML, GIST**
Gefitinib (Iressa: Astra Zeneca)	**EGFR, (ERBB4,GAK,…)**	**NSCLC**

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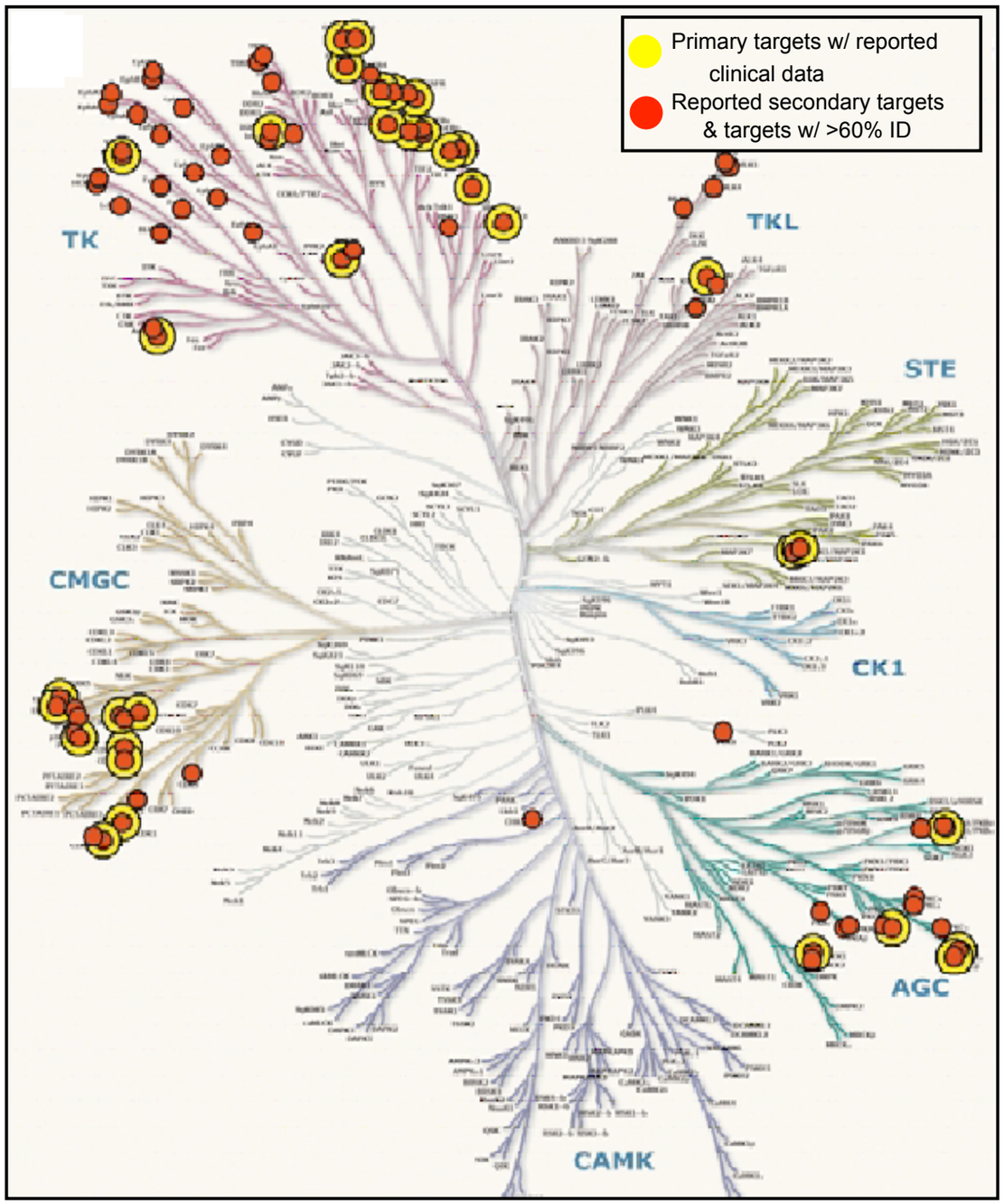
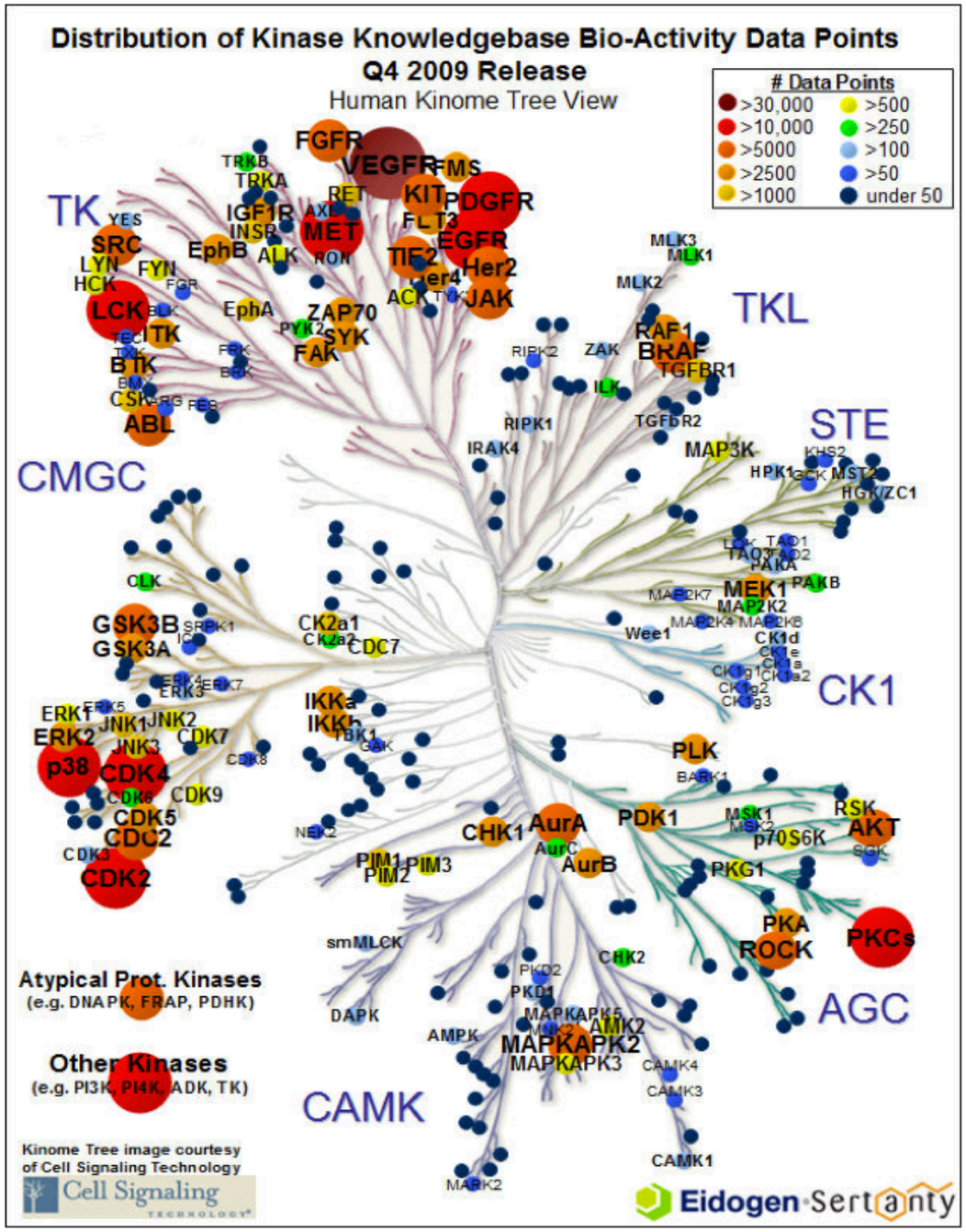
Background: Kinase Knowledgebase (KKB)

Kinase Targets of Clinical Interest

from Vieth *et al*. ***Drug Disc. Today*** **10, 839 (2005).**



Eidogen-Sertanty KKB SAR Data Point Distribution



> 507,000 SAR data points curated from
> 6250 journal articles and patents

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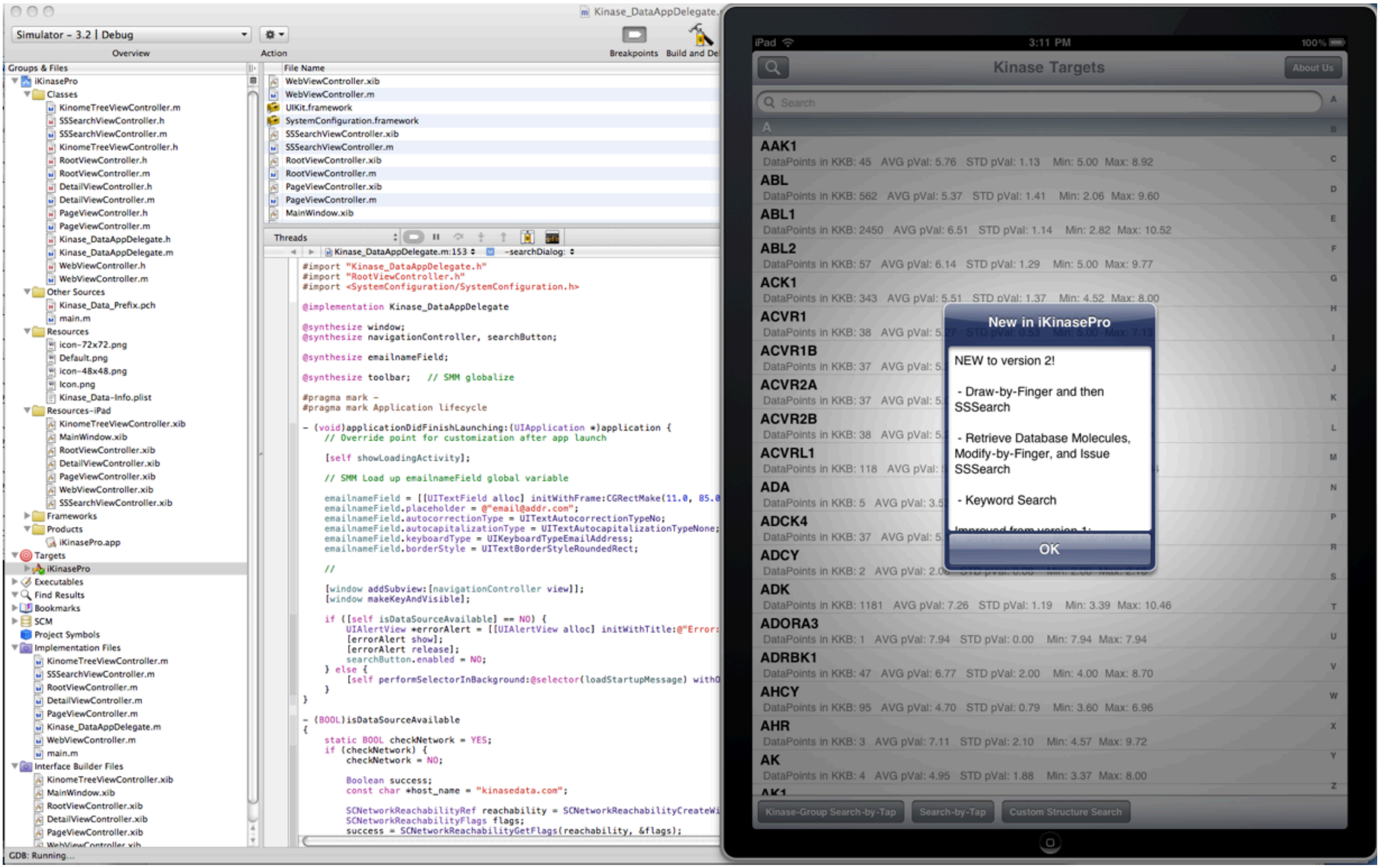
Infrastructure

- iPad w/Internet Connection (Wi-Fi or 3G)
- Database/WebServer (e.g. kinasedata.com: GoDaddy/HostGator)
  - Apache + php
  - mysql

- StructureSearch/Application Server (Amazon Cloud-LAMP)
  - Apache + php
  - mysql
  - ChemAxon JChem + JChemWebServices (includes tomcat/axis2, etc.)
  - Chemene JSDraw
- RICE.....

The iPad - A Revolutionary Device?

iPad - In Practice



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Cloud Computing - A Revolution?

Cloud Computing - In Practice

Amazon EC2 | Amazon Elastic MapReduce | Amazon CloudFront

Navigation

Region: US East

- EC2 Dashboard

INSTANCES
- Instances
- Spot Requests

IMAGES
- AMIs
- Bundle Tasks

ELASTIC BLOCK STORE
- Volumes
- Snapshots

NETWORKING & SECURITY
- Elastic IPs
- Security Groups
- Key Pairs
- Load Balancers

Amazon EC2 Console Dashboard

Getting Started

To start using Amazon EC2 you will want to launch a virtual server, known as an Amazon EC2 instance.

Launch Instance

Note: Your instances will launch in the US East (Virginia) region.

Service Health

Current Status	Details
Amazon EC2 (US East - N. Virginia)	Service is operating normally

View complete service health details

My Resources

You are using the following Amazon EC2 resources in the US East (Virginia) region:

Refresh

- 1 Running Instance
- 1 Elastic IP
- 1 EBS Volume
- 4 EBS Snapshots
- 2 Key Pairs
- 2 Security Groups
- 0 Load Balancers

Related Links

- Documentation
- All EC2 Resources
- Forums
- Feedback
- Report an Issue

Navigation

Region: US East

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INSTANCES
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My Instances

Launch Instance | Instance Actions | Reserved Instances | Show/Hide | Refresh | Help

Viewing: All Instances | All Instance Types

1 to 1 of 1 Instances

Instance	AMI ID	Root Device Type	Type	Status	Lifecycle	Public DNS	Security Groups	Key Pair Name	Mon
i-294bf742	ami-2cb05345	instance-store	m1.small	running	normal	ec2-184-73-205-197.compute-1.amazonaws.com	defaultLAMP	kinasedata	

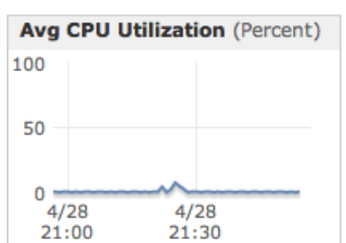
1 EC2 Instance selected

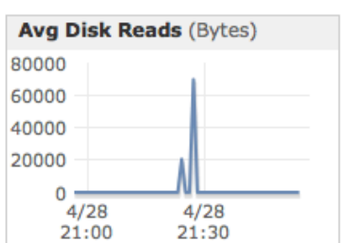
EC2 Instance: i-294bf742

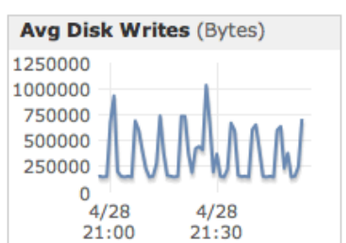
Description | Monitoring

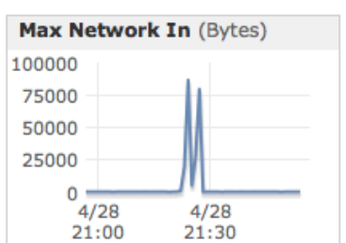
Graphs are for 1 instance that has monitoring enabled. Times are displayed in UTC.

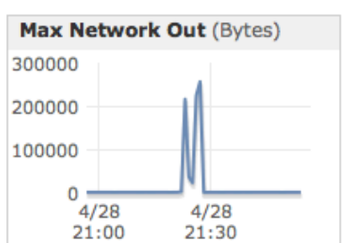
Time Range: Last Hour | Refresh











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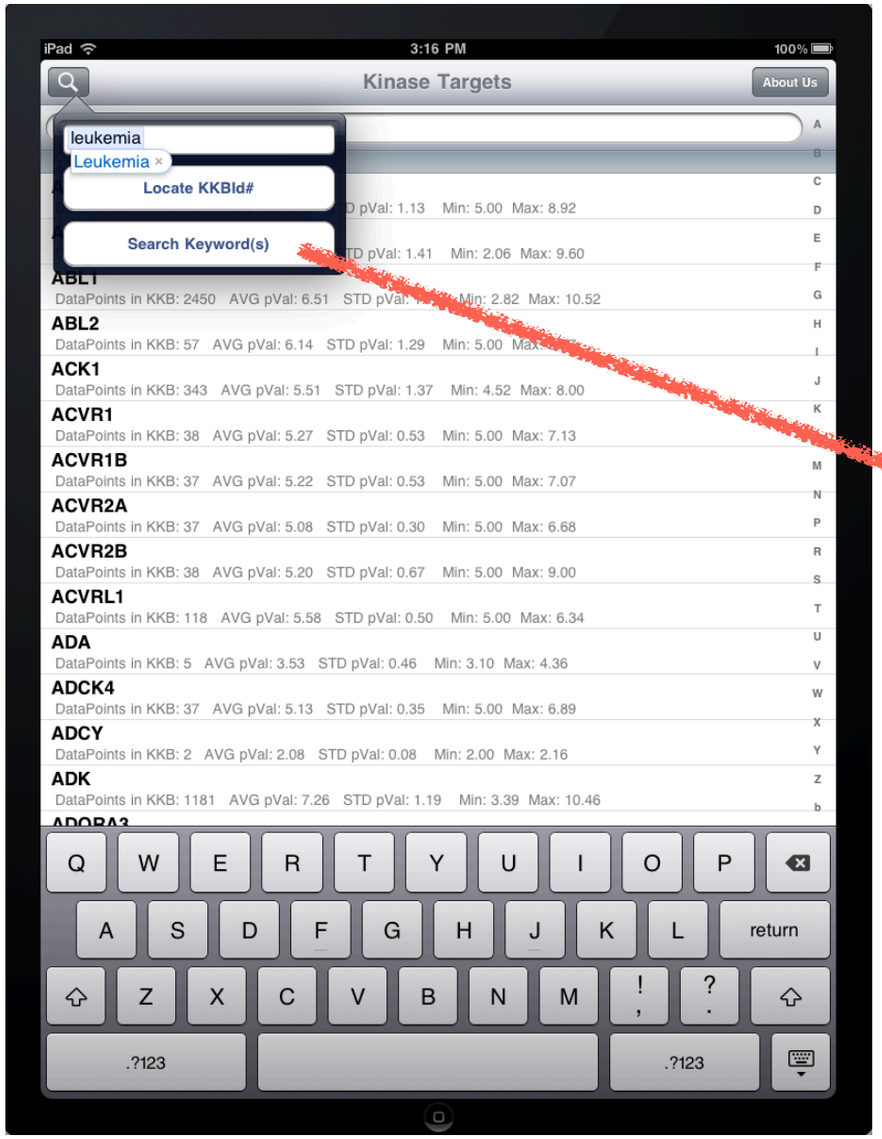
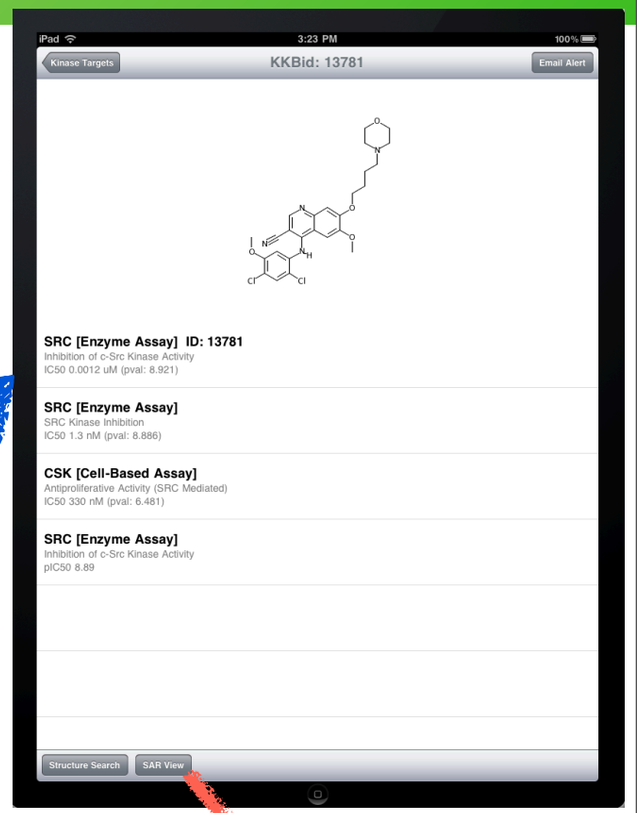
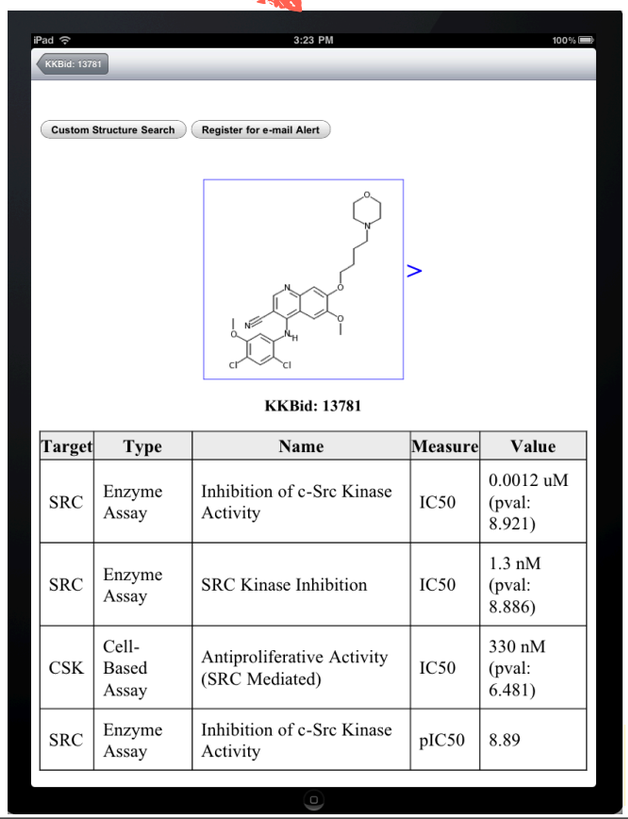
Amazon's Cloud Cost Example

		Totals
Amazon Elastic Compute Cloud		
View/Edit Service		
US East (Northern Virginia) Region		
Amazon EC2 running Linux/UNIX Reserved Instances		
$227.50 one-time fee per Small Instance (m1.small) for 1 yr purchased on 2010-04-01 at 08:00 GMT	1	227.50
- Payment received on April 1 - Thank you!	Payment	-227.50
$0.03 per Small Instance (m1.small) instance-hour (or partial hour)	655 Hrs	19.65
Amazon EC2 running Linux/UNIX		
$0.085 per Small Instance (m1.small) instance-hour (or partial hour)	8 Hrs	0.68
Amazon EC2 EBS		
$0.10 per GB-month of provisioned storage	9.208 GB-Mo	0.92
$0.01 per 1,000 puts (when saving a snapshot)	61 Requests	0.01
Amazon CloudWatch		
$0.015 per monitored instance-hour (or partial hour)	663 Hrs	9.95
	Download Usage Report »	**31.21**
Amazon Simple Storage Service		
View/Edit Service		
US Standard Region		
$0.150 per GB - first 50 TB / month of storage used	1.067 GB-Mo	0.16
	Download Usage Report »	**0.16**

Looking “Under the Hood”

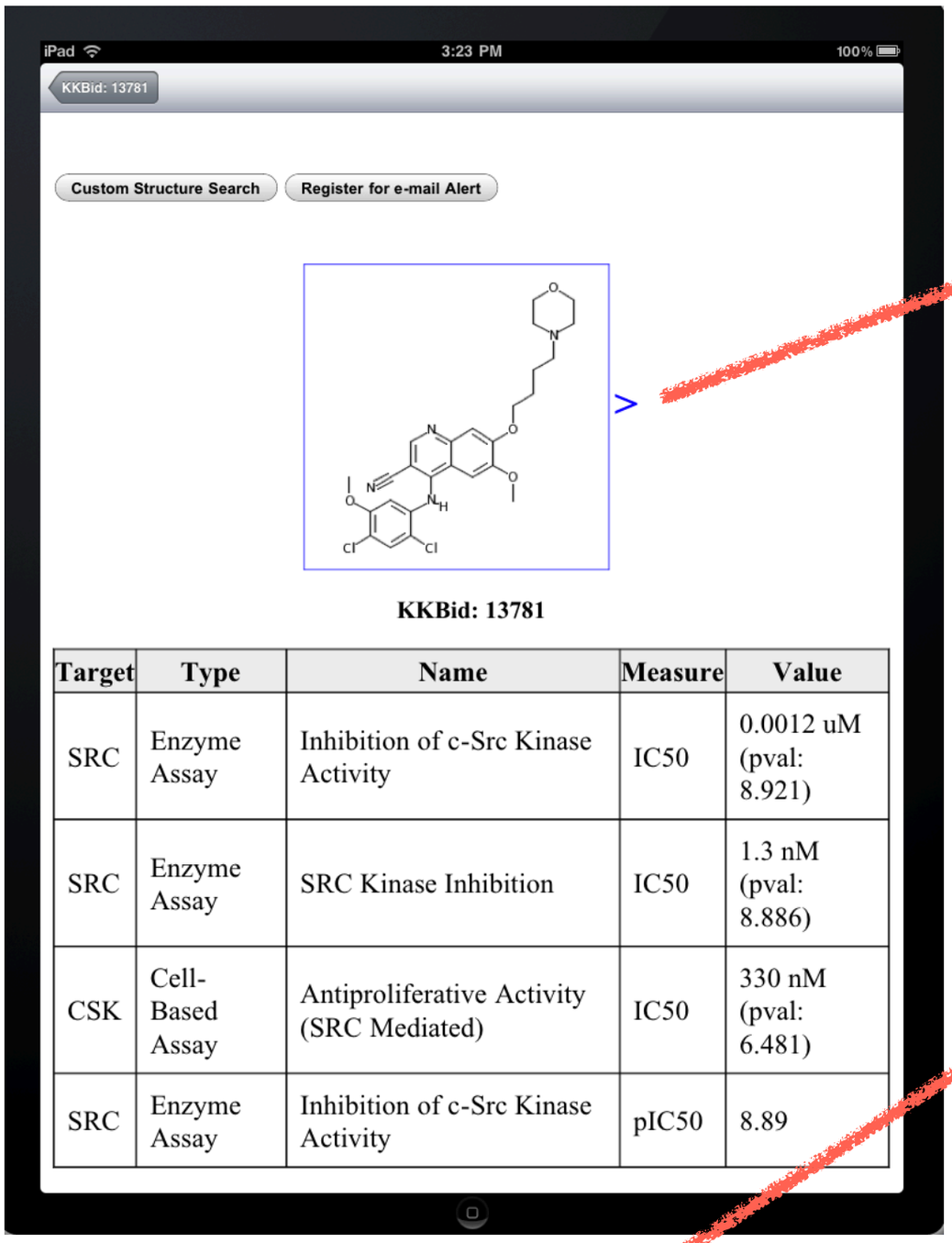


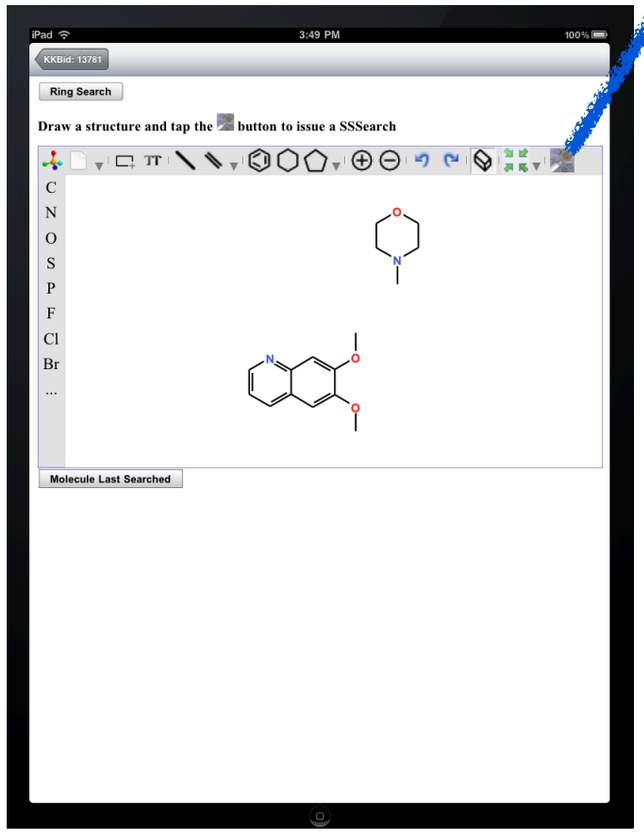


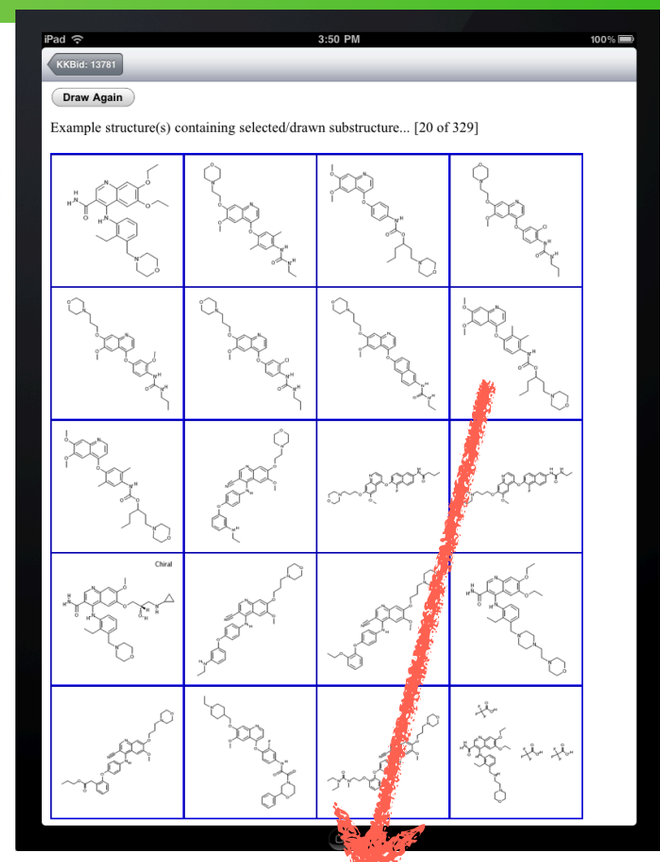


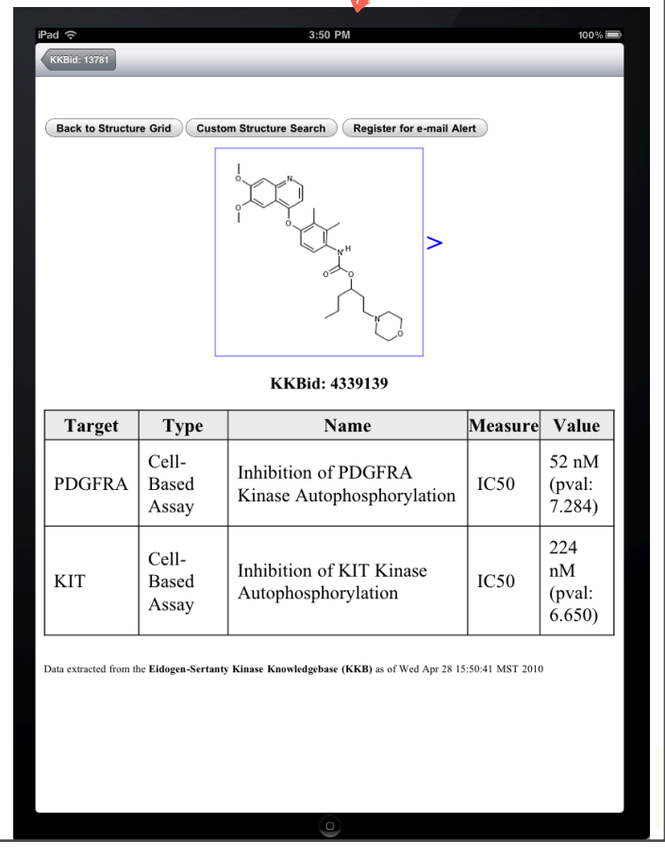
Target	Type	Name	Measure	Value
SRC	Enzyme Assay	Inhibition of c-Src Kinase Activity	IC50	0.0012 uM (pval: 8.921)
SRC	Enzyme Assay	SRC Kinase Inhibition	IC50	1.3 nM (pval: 8.886)
CSK	Cell-Based Assay	Antiproliferative Activity (SRC Mediated)	IC50	330 nM (pval: 6.481)
SRC	Enzyme Assay	Inhibition of c-Src Kinase Activity	pIC50	8.89

Looking “Under the Hood” (cont.)









Digging Even Deeper... php/SOAP/JChemSearchWS

```
$maxhits=20;
$soap = new SoapClient('http://myserver.com:8180/axis2/services/JChemSearchWS?wsdl');
$conn_param = array( 'driver' => 'com.mysql.jdbc.Driver',
            'url' => 'jdbc:mysql://myserver.com/mysqlDb',
            'username' => 'myusername',
            'password' => 'mypassword',
            'propertyTable' => 'JChemProperties');
 $result= strip_tags($soap->getConnectionAndTableInfo($conn_param)->return);
 $id=substr($result,0,strpos($result,"\n"));
 $search_param = array(  'connectionHandlerId' => $id,
             'tableName' => 'jchemmol',
            'queryMolecule' => $smi,
            'queryOptions' => 'sep=! t:s!maxHitCount:0!maxTime:60000!returnNonHits:n!',
            'beginIndex' => '0',
            'count' => $maxhits,
            'outputFormat' => 'smiles',
            'dataFieldNames' => 'mr_id',
            'hitColorAndAlignmentOptions' => '');
```

Setup

```
$search_result = $soap->runCompleteSearch($search_param)->return;
```

Search

```
$soap = new SoapClient('http://myserver.com:8180/axis2/services/ConnectionWS?wsdl');
$soap->close(array('connectionHandlerId' => $id));
```

Cleanup

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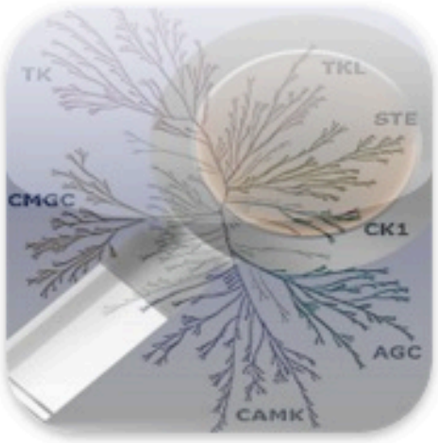
Application Availability

- iTunes and iPad AppStore

App Store › Medical › Eidogen-Sertanty



$9.99 Buy App

Category: Medical
Updated: May 06, 2010
Current Version: 2
0.3 MB
Language: English

iKinasePro

Description

iKinasePro brings the mobile kinome to a whole new level!

With iKinasePro not only do you gain access to the most recent release of the Eidogen-Sertanty's Kinase Knowledgebase (KKB), but you can also survey this large database with substructure-, similarity-, and super-similarity searches.

With the large iPad screen, we have introduced new "search-by-tap" functionality. Here, you can survey the kinome by tapping through a vast array of ring structures or search by aggregated kinase families by tapping on the kinome tree. You can also issue custom structure searches through finger-drawn substructures.

Within iKinasePro, you can also register for alerts to keep current with new KKB updates and receive detailed SAR information by email.

iKinasePro requires an internet connection.

Eidogen-Sertanty Web Site › **iKinasePro Support ›**

http://itunes.apple.com/us/app/ikinasepro/id364370393?mt=8

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Last Word... kinasedata.com

Kinase Data Portal

About Us | Hot Targets | Hot Articles | Support | Contact Us

Kinasedata.com, a webPortal encouraging kinase related discussion, community building and discussion. Users of the webPortal can freely see articles of interest, and engage in discussion. With free registration, users can obtain validation structure activity datasets for research activities.

Once registered in **Kinasedata.com**, students and academic institutions can purchase at a dramatically discounted price a newly released version of the Kinase Knowledgebase (KKB™) – Academic Edition.

iKinase, is the Kinome on the go. The apps are available through the iTunes store for iKinase and iKinase Pro.

Kinase Knowledgebase (KKB™), a small molecule activity data is manually curated by a experienced team of PhD chemists and biologists from patents and peer-reviewed publications. The Q4-09 release covers 6,251 journal articles and patents with 20,593 assay protocols including 162,000 SAR data points and 400 unique targets. KKB™ incorporated a number of concepts by which the data is organized including standardized HUGO gene targets where possible. The data is available in a variety of formats including an Instant JChem structure searchable database. In addition to the data as published we now also offer KKB™ for QSAR and modeling. In this KKB™ version high-quality concentration response end points of biochemical assays are aggregated by unique chemical structures across assay protocols and unique HUGO kinase targets and the end points are reported as p-values. The aggregated release of KKB™ does not require any pre-processing or further standardization and can directly be used to develop QSAR or categorization models.

iKinase Pro

We are happy to announce iKinasePro for the iPad!

iKinasePro brings the mobile kinome to a whole new level! With iKinasePro not only do you gain access to the most recent release of the Eidogen-Sertanty's Kinase Knowledgebase (KKB), but you can also survey this large database with substructure-, similarity-, and super-similarity searches. With the large iPad screen, we have introduced new "search-by-tap" functionality...

iKinase v2

We are happy to announce iKinase version 2 (update 1)!

iKinase provides sample structure activity data from Eidogen-Sertanty's Kinase Knowledgebase (KKB). With iKinase, a user
can search for Kinase targets by standardized names, identify top-active molecules for each target, and drill-down into more detail...

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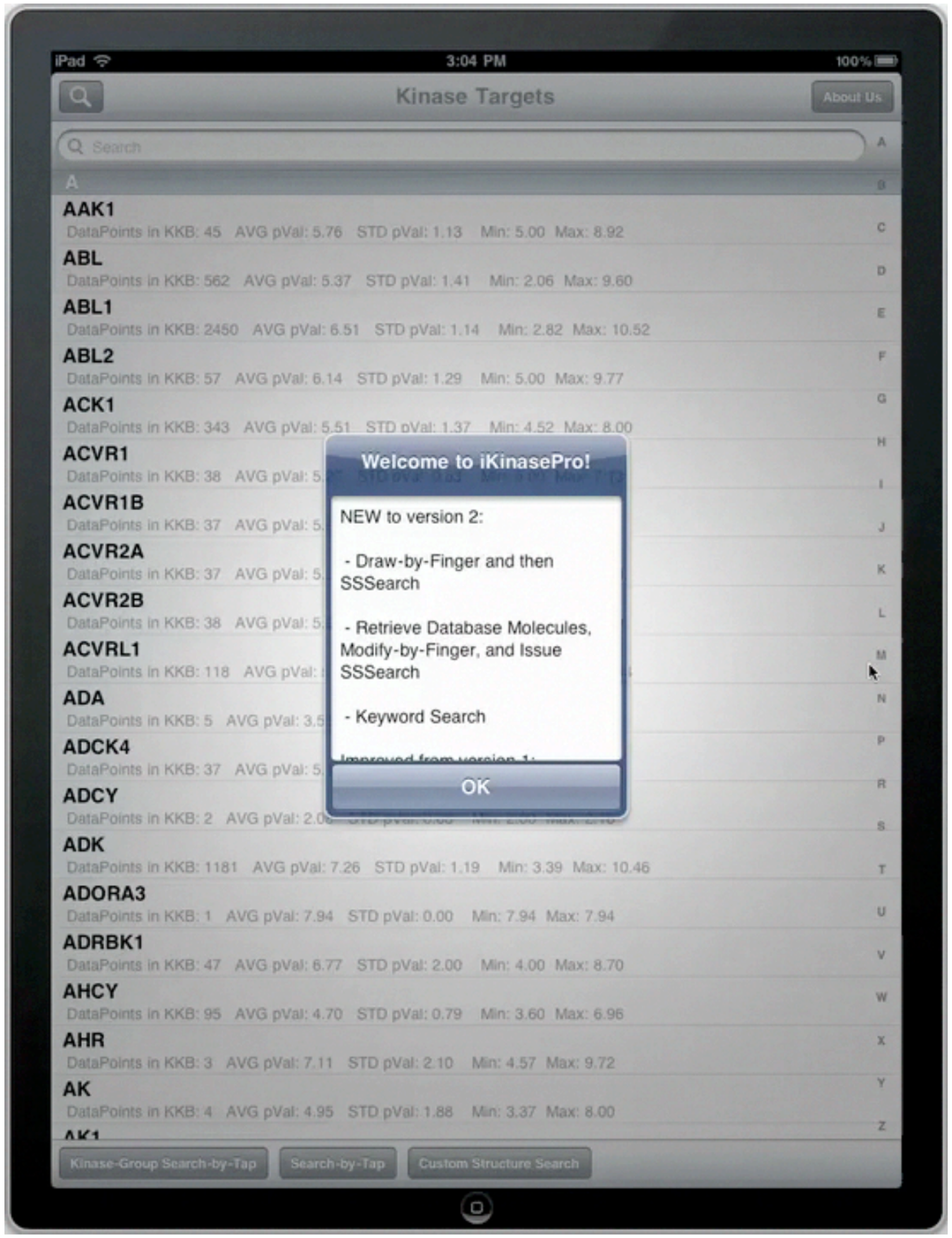
Nagyon köszönöm!

Draw Search Demo



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