

Dx Innovation in Decline? An Empirical Analysis post- *Mayo*

Colleen V. Chien, Santa Clara University Law School
Arti K. Rai, Duke University Law School



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Motivating Question

Have decisions making it more difficult to patent diagnostics resulted in a **decline** in innovation beginning in 2012? See *Bilski*, 2010 *Mayo v. Prometheus*, 2012

Caveats: innovation needs to be proxied by various imperfect measures; also reimbursement changes, other initiatives create noise

Motivating Question

Have decisions making it more difficult to patent diagnostics resulted in a **decline** in innovation beginning in 2012?

Testable Hypotheses (so far, others to come . . .)

- Innovation (as proxied by patent filings) has **declined**
- Patent scope has **narrowed**, benefiting future innovators at the cost of current innovators

Motivating Question

Have decisions making it more difficult to patent diagnostics resulted in a **decline** in innovation beginning in 2012?

What we considered:

- The **amount** of innovation (*patent apps*)
- The **scope** of protection (*patent claims*)
- The **market** for innovation (*transactions*)

Approach

1. Considered innovation before and after *Mayo*.
 - a. Published Patent Applications
 - b. Material Transactions reported to the SEC
2. In applications, compared Dx innovation with “control group” of enabling tech innovation.
3. Impact on patentable scope - narrower?

Dx Innovation vs. “control group”

- 1) “Dx” Innovation - biomarker *correlated* to medically relevant utility.
(e.g. CPC class G01 2800 -- diagnosing and detecting disease -- other CPC classes include 12Q1/68; 12Q1/70; most of C12Q2600). ~31K apps
- 2) “Enabling Tech” control group - similar but more “upstream” analysis of genes, gene expression -- likely no clinical utility (e.g. C12Q2539; C12Q2561; G06F/10-24). ~6K apps

Latter a good “control group”

Caveats: perhaps some overlap in categories; “enabling tech” could be affected by *Bilski* (2010) and *Alice* (2014)

Additional Assumptions, Methods, and Weaknesses

1. Identified precision medicine patents/apps based on CPC filed before and after *Mayo* through 12/31/2014 and published since then (some truncation in 2015 data due to non-pub requests). But class-based schemes are limited. *Mayo* and associated USPTO guidance came out in mid-2012 so we treated **2011 as a baseline and looked for impact in applications starting in the second half of in 2012**. However, effect may be more lagged. Also other important, intervening policy (e.g. President's PMI, reimbursements policy) and developments contribute to lack of clean "treatment" effect.
2. Used KtMine for publicly recorded agreements, a proprietary datasource limiting replicability. Relied on PatentsView and Innography as well.
3. Limited ability to measure any shift to non-patent innovation (TS) (though looked at agreements).
4. Used 1st claim word count as a proxy for claim scope.
5. Work in progress!

Motivating Question

Have decisions making it more difficult to patent diagnostics caused innovation to **decline**?

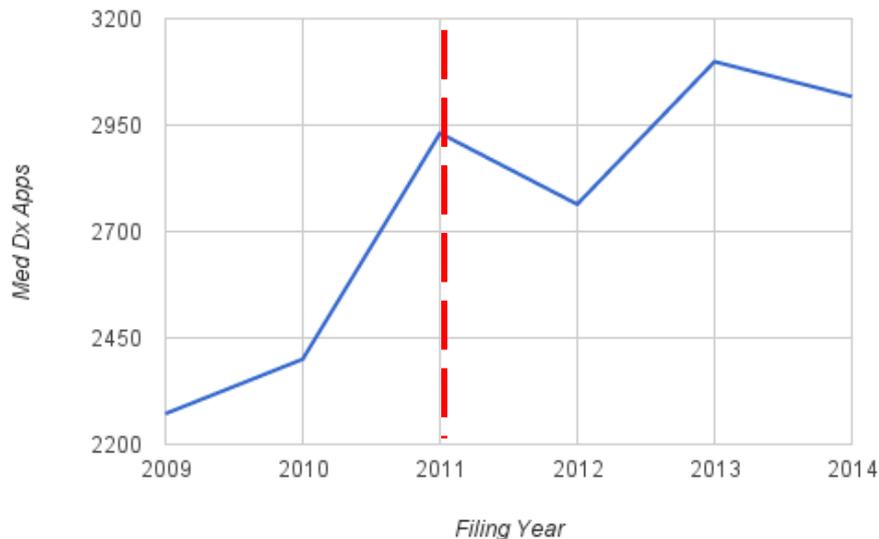
What we considered:

- The **amount** of innovation
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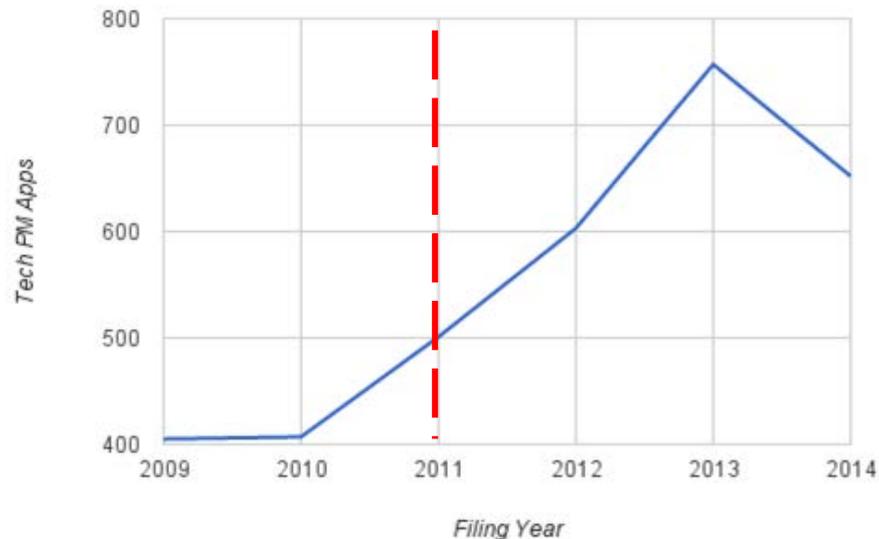
Has innovation declined?

Finding: Dx apps declined and then recovered (2014 truncation). Tech Apps rose and in 2014, declined slightly.

Core Dx Apps vs. Filing Year

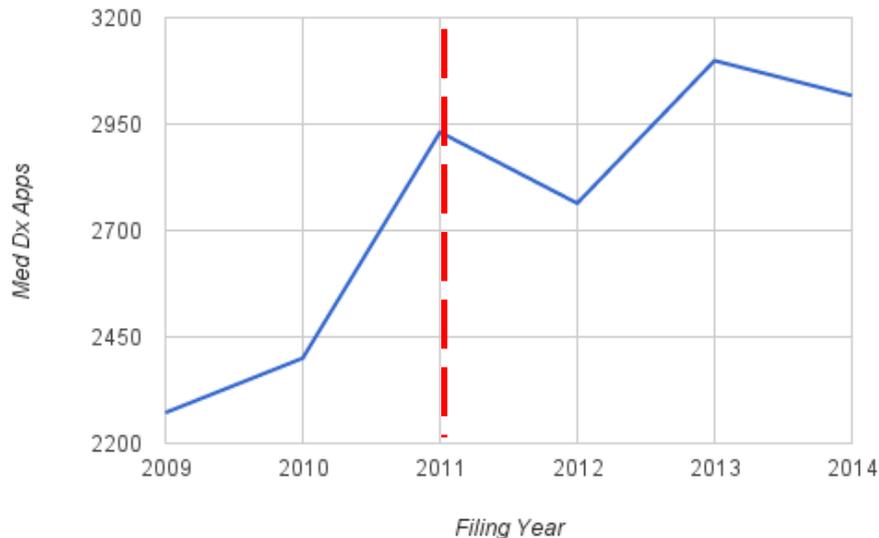


Tech Apps vs. Filing Year



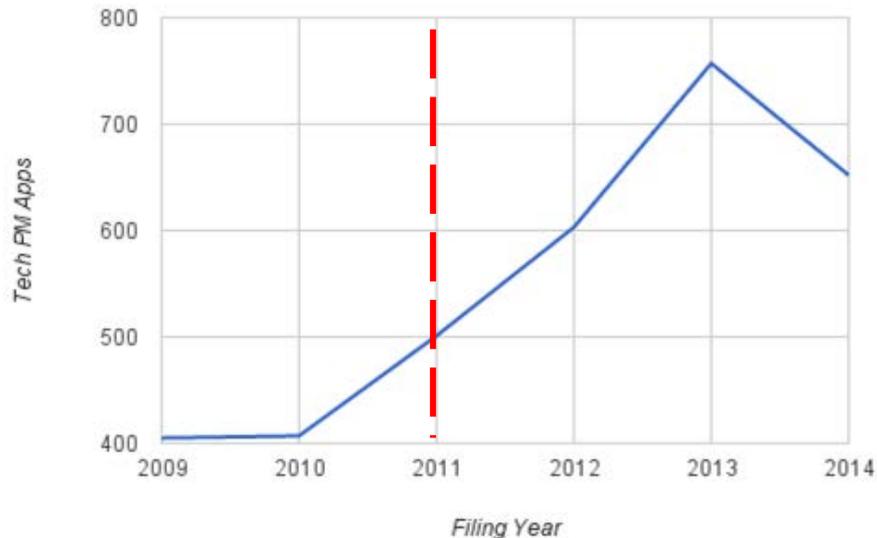
Finding: Dx apps have grown more slowly than Tech enabling apps

Core Dx Apps vs. Filing Year



+3% increase since 2011

Tech Apps vs. Filing Year



+8% increase since 2011

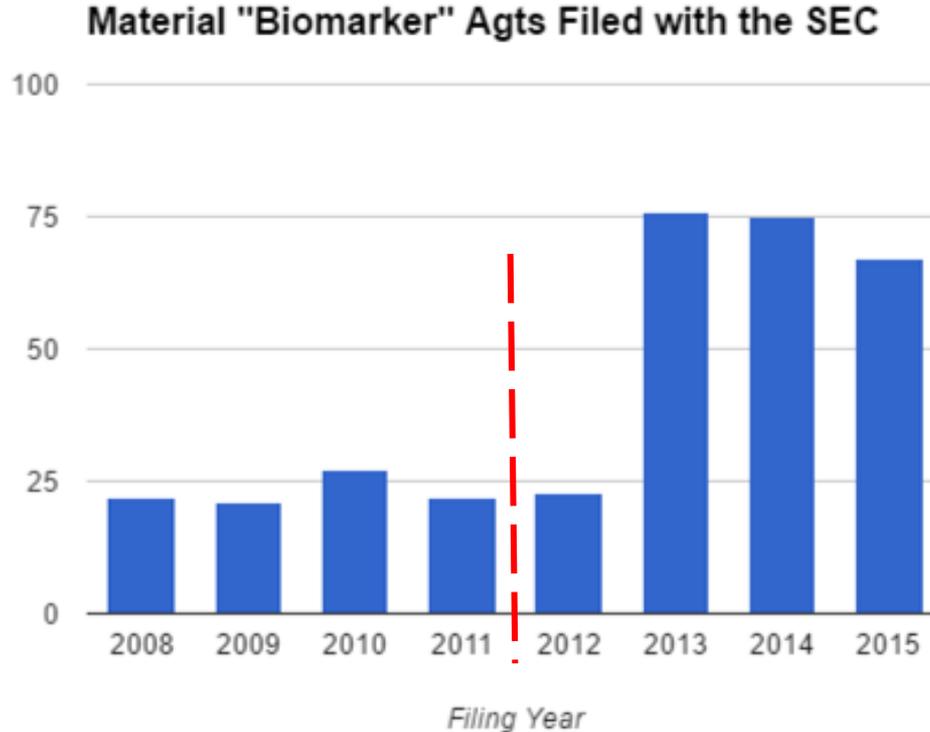
Are patent apps significantly down since 2011, indicating that innovation may have **declined due to Mayo?**

No clear effect

- *Core Dx applications dipped in 2012 but appear to have recovered since.*
- *But control group of enabling tech applications did grow faster (declined in 2014 but are still up since 2011); (2014 decline may be due to truncation effects and 2014 Alice decision)*

Has there been a **decline** in innovation, measured by material transactions?

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Has there been a **decline** in innovation, measured by material transactions?

No,

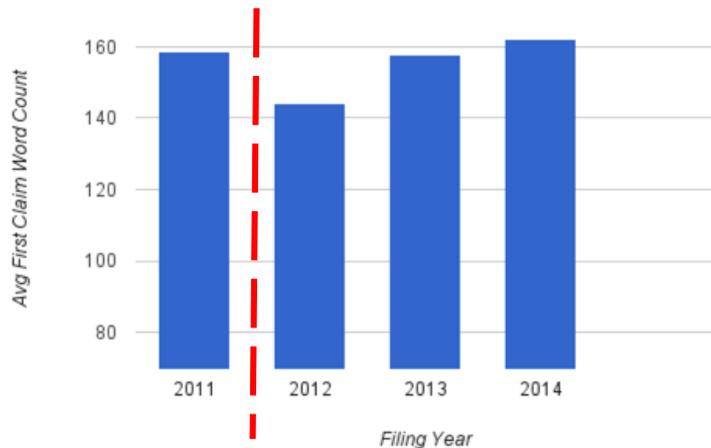
Recorded “biomarker” transactions are up.

Has the scope of protection **narrowed**?

Finding: The number of words per first claim has increased more among core Dx patent applications than among enabling tech patent apps

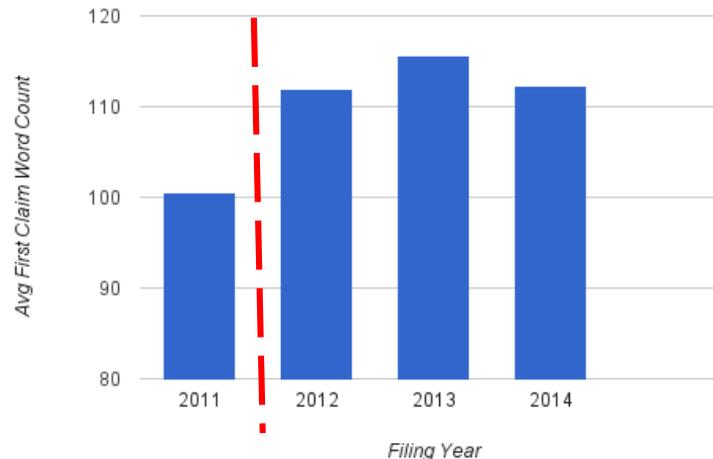
Patent App Avg 1st Claim Length

Enabling Tech Patent Apps



+2% increase since 2011

Core Dx Patent Apps



+12% increase since 2011

Has the scope of protection **narrowed**?

Yes,

1st claims of 2014-filed Core Dx apps are, on average, 12% longer than 1st claims of 2011-filed apps. (2014-filed Enabling Tech app first claims are only 2% longer)

Summary

We looked for **clear evidence of a sustained decline** in diagnostic patent applications and transactions post-Mayo. **We didn't find it.**

- Patent filings are up.
- Transactions are up.

However

- Impact on commercial firms may be muted in these overall numbers which include large shares of nonprofit parenting.
- Some evidence that CoreDx apps growing more slowly than control group
- Claims are longer (narrower).
- Effect may be lagged / impact may be forthcoming.
- IP-centric business models in Dx now less attractive.
- Reimbursement regime changes may overshadow patent changes.
- Our work is ongoing.

Thank you

Colleen Chien

colleenchien@gmail.com



colleen_chien

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PatentsView, KtMine, AIR

BACKUP SLIDES

CPC Definitions

Core Dx

C12Q 1/68, C12Q 1/70, G01N 2800, G01N 33/569, G01N 33/571, G01N 33/574, C12Q 2600/106, C12Q 2600/112, C12Q 2600/118, C12Q 2600/142, C12Q 2600/154, C12Q 2600/156, C12Q 2600/158, C12Q 2600/16, C12Q 2600/172

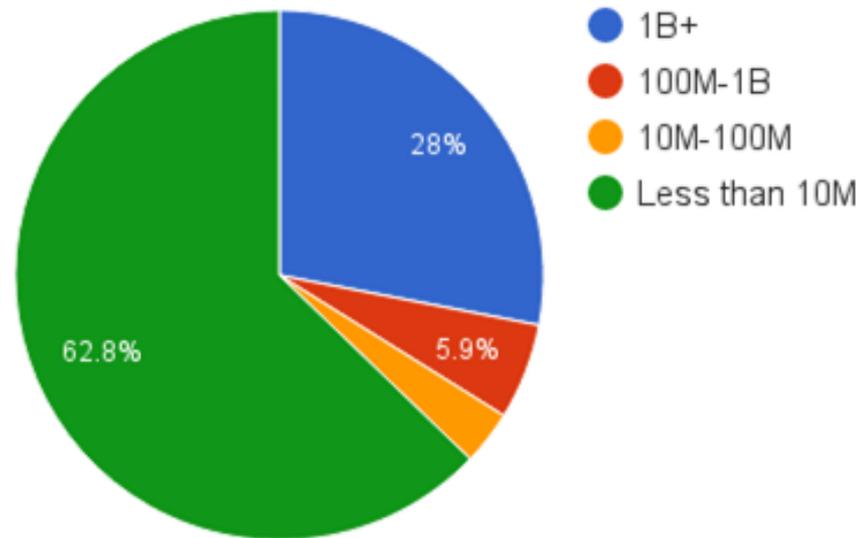
Enabling Tech

C12Q 2539, C12Q 2561, G06F 19/10, G06F 19/12, G06F 19/14, G06F 19/16, G06F 19/18, G06F 19/20, G06F 19/22, G06F 19/24

Dx is dominated by universities and nonprofits, who are five of the top 10 patentholders.

<u>Top Core Dx Patentholders</u>	<u>Number of Apps</u>
Roche Holding Ltd.	1691
University Of California	506
Thermo Fisher Scientific Inc.	500
Geneasys Pty Ltd	355
Partners Healthcare Sys, Inc., Mass.	344
Johns Hopkins University	331
HHS	293
Stanford University	276
Takeda	220
Glaxosmithkline Plc	219

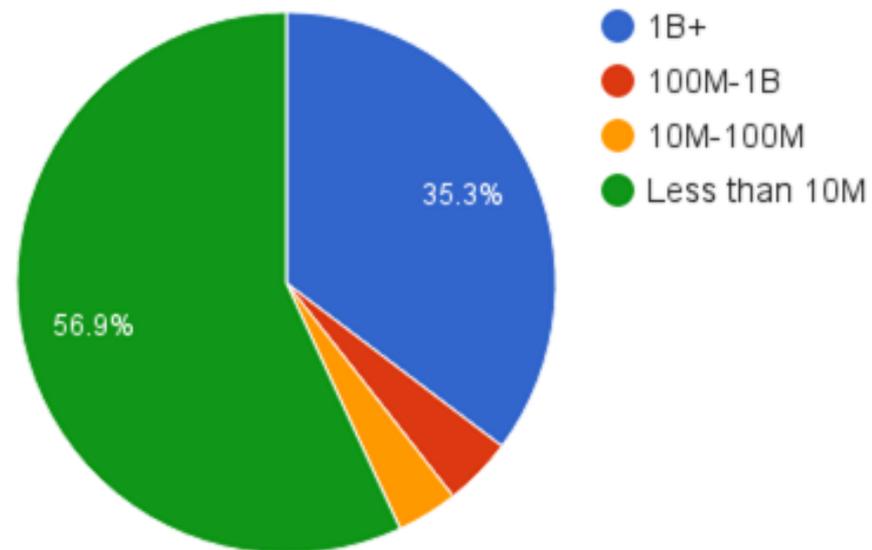
Core Dx Apps by Filing Firm Revenue



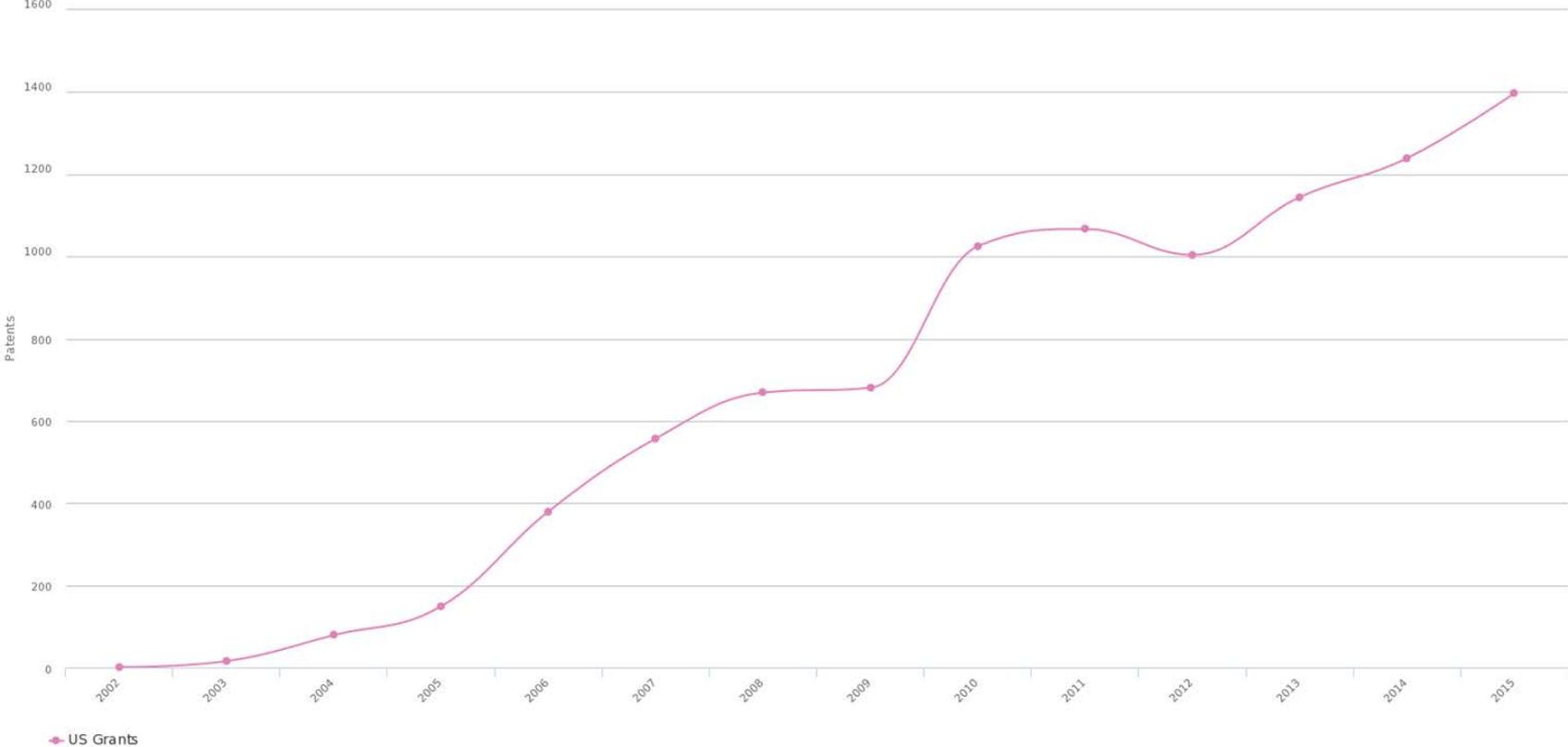
Instrument and tech companies lead **enabling tech**, though entities with less than \$10M in revenue still dominate.

<u>Top Enabling Tech Patentholders</u>	<u>Number of Apps</u>
Thermo Fisher Scientific Inc.	569
Agilent Technologies Inc.	149
IBM	133
University Of California	93
Roche Holding Ltd.	72
Hitachi, Ltd.	70
Aliph, Inc.	68
Illumina, Inc.	64
Abbott Laboratories	52
Expense Bioinformatics, Inc.	50

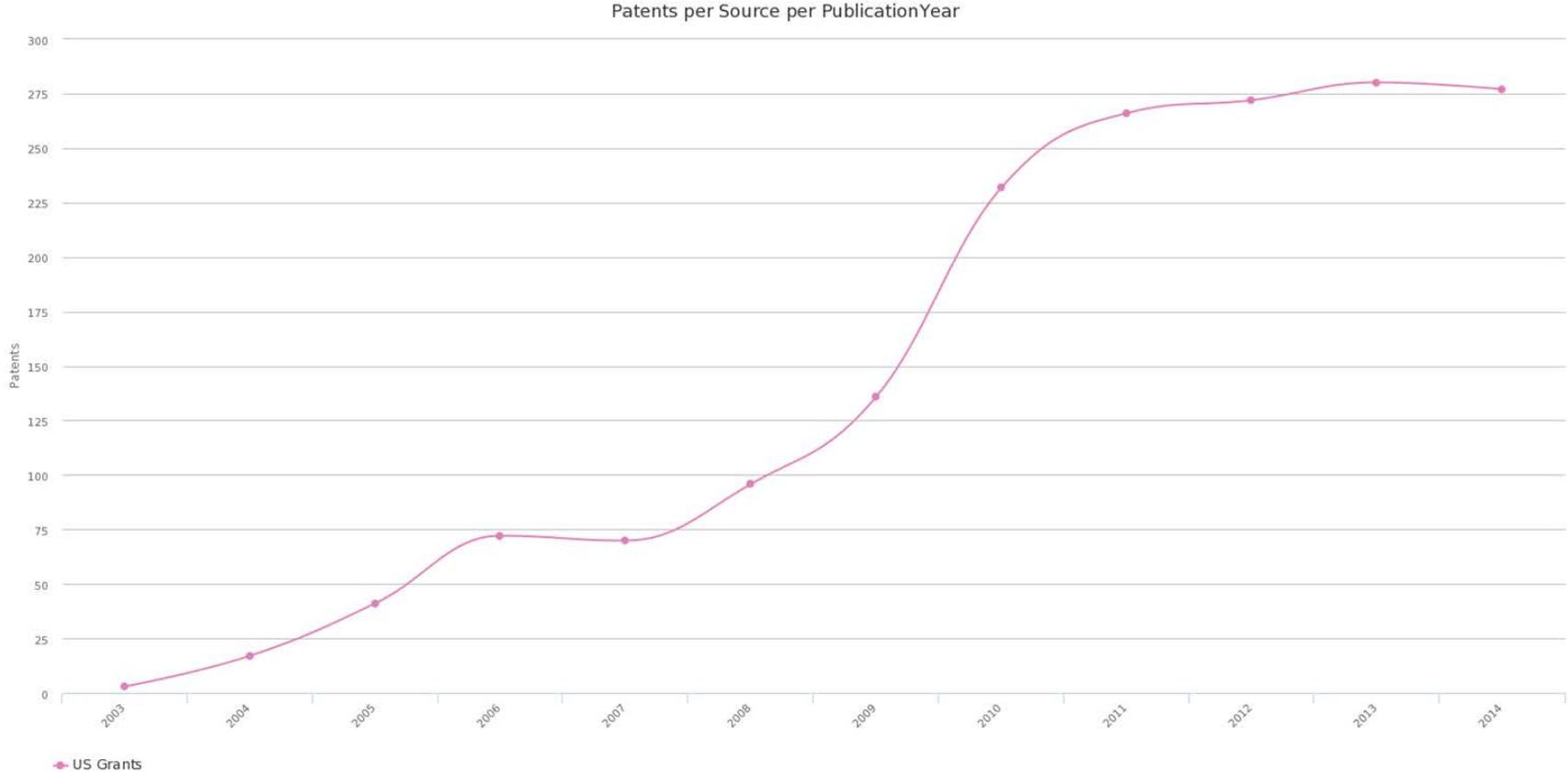
Enabling Tech Apps by Filing Firm Revenue



Finding: Core Dx grants have grown.



Finding: Enabling Tech PM grants have leveled off.



Measure narrowing through longer claims

Patent 8,906,625 (“genes involved in estrogen metabolism”)

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1. A method of predicting the likelihood of cancer recurrence for a human subject diagnosed with breast cancer, comprising:
 - assaying a level of an RNA transcript of voltage-dependent anion channel 1 (VDAC1) in a tumor sample obtained from said subject **using a primer comprising a nucleotide sequence selected from SEQ ID NO:334 and SEQ ID NO:335**; normalizing the level of an RNA transcript of VDAC1 against the expression level of one or more reference genes to obtain a normalized expression level of VDAC1; using the normalized expression level of VDAC1 to generate information comprising a prediction of cancer recurrence for said subject, wherein the normalized expression level of VDAC1 is positively correlated with an increased likelihood of cancer recurrence.
-
- Filed in 2010
 - Bolded language overcame *Mayo* rejection (“examiner comments”)

Patent No. 8,765,383 (“methods of predicting cancer risk using gene expression in premalignant tissue”)

1. A method for determining cancer risk for a human patient, comprising: **analyzing a sequence of BRAF in a tissue sample obtained from a premalignant lesion from the lower gastrointestinal (GI) tract of the patient to detect a V600E mutation**; measuring a level of an RNA transcript of DUSP6, or its expression product, in the tissue sample; normalizing the level of the RNA transcript of DUSP6, or its expression product, against an expression level of at least one reference gene, to obtain a normalized expression level of DUSP6, comparing the normalized expression level of DUSP6 from the patient to the normalized expression level of DUSP6 in a population with no cancer; and determining that the patient has an increased cancer risk if the normalized expression level of DUSP6 from the patient is increased, or that the patient has a decreased cancer risk if the normalized expression level of DUSP6 from the patient is decreased.

- Bolded language overcame *Mayo* rejection
- *European counterpart* (intention to grant announced) (EP2417271)
- For EPO, limitation of “sequence of BRAF from biological sample to detect a V600E mutation” introduced in dependent claim ONLY