Intellectual Property in Precision Medicine

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(with Colleen Chien)
Supreme Court “Section 101” decisions


- Step 1: Does the patent claim encompass: law of nature; product of nature; abstract idea
- Step 2: If so, does it have an “inventive concept” or “additional elements” that go beyond unpatentable law of nature, product of nature, abstract idea
The View from Lawyers

Since 2012, a series of U.S. Supreme Court decisions...have left innovators in the biotechnology and software industries unable to secure patent protections for many of their inventions. Since patents play a critical role in driving innovation, these decisions have potentially far-reaching implications for the U.S. economy.
A majority [of participants][1] recommended legislative change. A call for legislation was particularly strong from the life sciences industry but also had many supporters from computer-related industries. According to these participants, the Court’s precedent is having such a harmful impact on innovation and business development that a legislative solution is critical.
nearly all of the conferees recognized that this state of the law poses serious concerns for bioscience research and development.
Also . . .

- Regulatory uncertainty
- Reimbursement challenges
Motivating Question

How have Court decisions, other uncertainty affected patenting behavior and other metrics?
Caveats

1) Metrics not (necessarily) the same as innovation

2) Because of regulatory, reimbursement complications in time frame, cannot make causal claims regarding impact of Court decisions

3) Various time lags
Metrics

Patent app counts (and patent scope) (treatment vs control)

SEC “Biomarker”

FDA Approvals
“Med Dx” CPCs (biomarker correlated to medically relevant utility)

- G01N2800: Detection or diagnosis of diseases (not including disease caused by micro-organisms where the micro-organism is detected); G01N33/569 (detection of bacteria, viruses); G01N33/571 (detection of venereal disease); G01N33/574 (cancer detection)
- C12Q1/6883 and C12Q1/6886 (using nucleic acids to test for disease) (biggest category; 96% true positive)
- C12Q2600/106, 112, and 118 (short nucleic acid sequences used for characterizing disease)

“Control” CPCs (TC 1600 generally)

Focus on impact of Mayo
Assuming immediate impact, how soon would we see impact?

- **March 2012 Mayo Decision**
- **4-12 Month Agreement Lead Time**
- **22-36 Months of Development**
- **18 Months Patent Publication**
- **12-24 Months FDA Approval Time**
No absolute decline in US Med Dx apps

Fig. 1: US Diagnostic Patent Applications and Grants
No relative decline in US Med Dx apps (vs. TC1600)

Fig. 2: US Diagnostic as a Share of All TC1600 (Biotechnology) Patent Applications
However growth has been uneven across segments... while filings by nonprofits and large companies have grown...

Fig. 3: US Diagnostic Patent Applications by Revenue

Publication Year
Firms with $1M-$100M in revenue have experienced uneven growth/slight declines

Fig. 4: US Diagnostic Patent Applications and Grants of Firms with $1M-$100M in Revenue
Has the scope of US protection *narrowed*, relative to the EPO?
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")
US8765383 ("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
Finding: Avg 1st claim length has increased in the PTO and EPO (more in PTO)

**Issued Patent Avg 1st Claim Length**

![Graph showing the average first claim length from 2008 to 2016 for Med Dx Grants (US) and Med Dx Grants (EP).](image)

- **Med Dx Grants (US)**  
  - Avg First Claim Word Count  
  - 2008: 100  
  - 2009: 120  
  - 2010: 120  
  - 2011: 120  
  - 2012: 250  
  - 2013: 120  
  - 2014: 120  
  - 2015: 120  
  - 2016: 120

- **Med Dx Grants (EP)**  
  - Avg First Claim Word Count  
  - 2008: 100  
  - 2009: 100  
  - 2010: 100  
  - 2011: 100  
  - 2012: 140  
  - 2013: 100  
  - 2014: 100  
  - 2015: 100  
  - 2016: 100

- **18% increase since 2011**
- **13% increase since 2011**
Has the scope of US protection narrowed, relative to the EPO and the pre-treatment period?

*Both EPO and US issued claim lengths are growing; US claim length has grown more than EPO claim length*
Is it easier to get a Dx patent in Europe than in the US now?

*No clear evidence*

*Abandonment/withdrawal rates among the European twin within the pair is higher than the abandonment/withdrawal rate among the US twin. However time effects make the sample size too small to draw strong conclusions.*
How has 101 caselaw impacted US prosecution rel to EPO prosecution?

Preliminary results based on case study of 10 resolved cases in the EPO and USPTO, 7 with 101 rejections

EPO outcome re 7
- 4 grants
- 3 withdrawals, bases:
  --- 53(c) (subject matter)*
  --- inventive step
  --- novelty + unity of invention

USPTO outcome re 7
- 5 grants
- 2 withdrawals (based on 101)
Has there been a decline in innovation, measured by material transactions?
Has there been a decline in innovation, measured by material transactions?
Has there been a decline in innovation, measured by material FDA Approvals?

Fig 7A: FDA Device "Diagnostic" Approvals - All
Has there been a *decline* in innovation, measured by material transactions or approvals?

*No clear evidence*

*Recorded “biomarker” transaction and approvals are up.*
Tentative Conclusions

- Large firms, nonprofits continue to file
- Some decline for smaller firms
- Scope has narrowed more in US than EU
- Unclear if it’s easier to get patent in EU
- Biomarker agreements, approvals up (but lag problem for approvals)