PATENTANWÄLTE

Patenting Biotech Inventions in the U.S. post Myriad and Mayo

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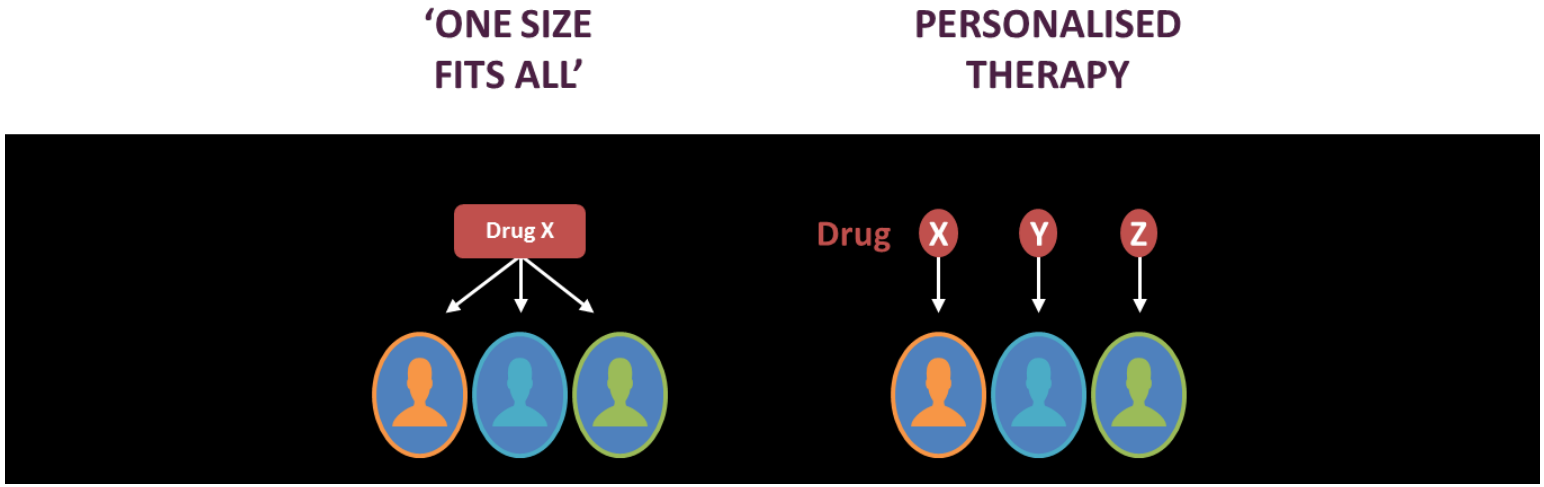
Dr. Jörk Zwicker

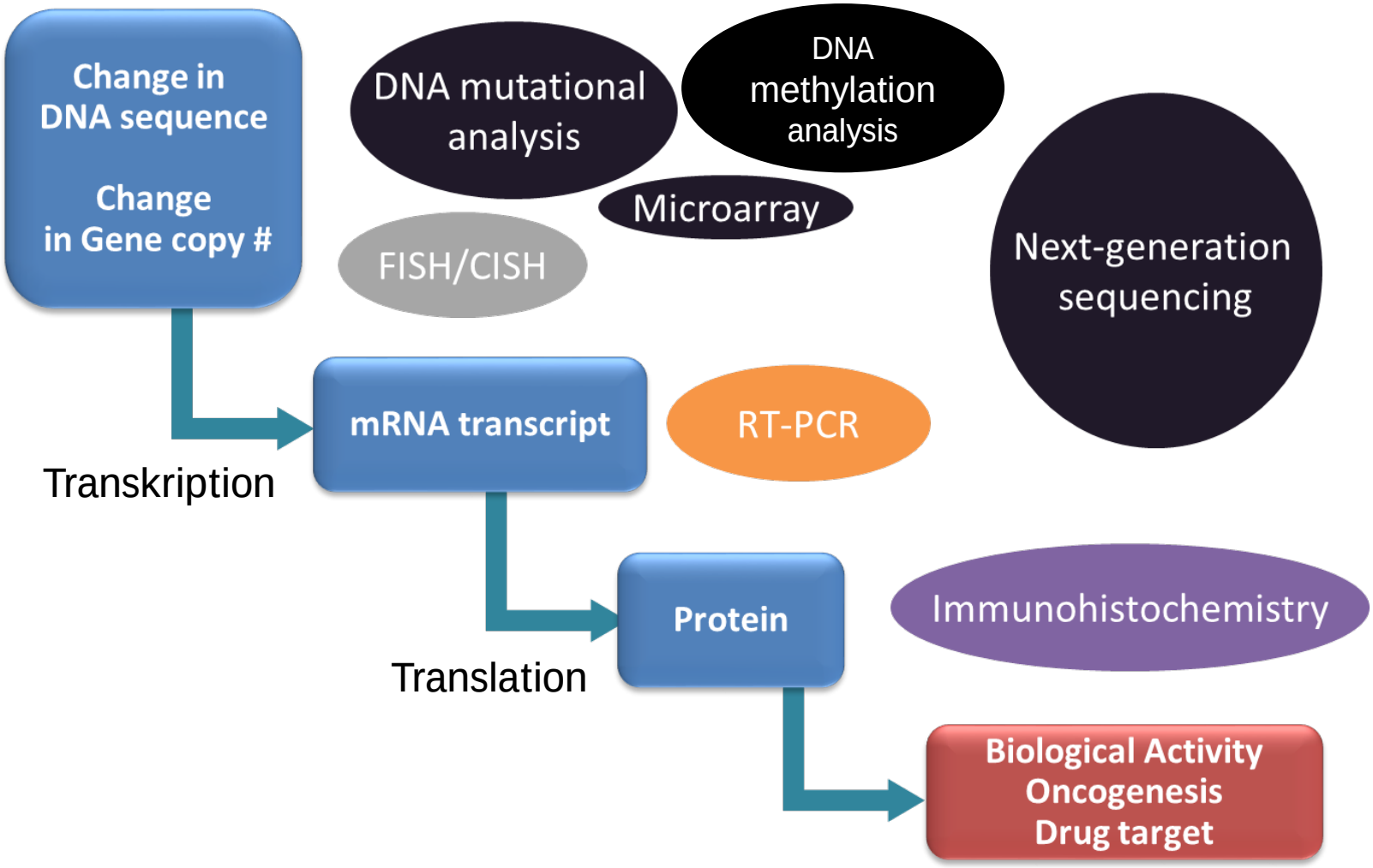
Personalized Medicine

Understanding the molecular basis of diseases has identified markers of diseases (diagnosis), drivers of diseases (prognosis) and allowed for sub-classification of diseases (prediction)



- **Diagnostic biomarker** allows detection of disease
- **Prognostic biomarker** indicates the likely course of disease in an untreated patient
- **Predictive biomarker** identifies patients that are most likely to benefit from a given therapy

Methods of Biomarker Analysis



Claiming Inventions in Personalized Medicine

Claim categories

- Substance protection for biomarker, biomarker specific diagnostics or biomarker specific therapeutics
- Method claims for diagnostic, predictive or prognostic methods
- Method of treatment (at the U.S.-PTO)/Second medical use (purpose limited substance claims at the EPO)

Substance Protection

- DNA, e.g. bisulfit converted CpG methylated genomic DNA
- RNA, e.g. miRNAs
- Proteins, e.g. disease specific splice variants of known proteins
- Antibodies, that specifically bind to therapeutic or diagnostic biomarkers
- Small molecules that specifically interact with therapeutic biomarkers

Diagnostic, Prognostic and Predictive Methods

- Method for diagnosing a disease by detecting presence or absence of a diagnostic biomarker in a sample.
- Method for prognosing, whether a healthy person will generate a disease or the course of disease by detecting presence or absence of a prognostic biomarker in a sample.
- Method for predicting, whether a patient is suitable to be treated with drug X by detecting the presence or absence of a predictive biomarker in a sample.
- Method for predicting, whether a patient will benefit from treatment after treatment with drug X by detecting the presence or absence of a predictive biomarker in a sample.

Methods of Treatment

- Method of treating a patient by administering a drug X, wherein the patient is selected as having disease Y
- Method of treating a patient by administering a drug X, wherein the patient is characterized by presence or absence of a prognostic biomarker

Patent Eligible Subject-Matter

35 U.S.C. 101

„Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.“

What is Patent Eligible Subject Matter?

Any new and useful:

- Process
- Machine
- Manufacture or composition of matter or improvement thereof
- "Anything under the sun made by man"

➔ Unpatentable subject matter (**judicial exceptions**)

- Products of nature ➔ AMP v. **Myriad** Genetics
- Laws of nature ➔ **Mayo** v. Prometheus
- Mathematical algorithms

AMP v. Myriad Genetics
Subject Matter Eligibility of Products

- *BRCA1* and *BRCA2* are genes that account for most inherited forms of breast and ovarian cancer.
- Myriad's genetic test identified women at increased risk of suffering from breast or ovarian cancer.
- Two types of claims were at issue:

  (i) composition claims directed to isolated DNA molecules;

  (ii) composition claims directed to cDNA
- Court found that isolating DNA molecules was not sufficient to confer patent eligibility, because "Myriad did not create or alter any of the genetic information encoded in the *BRCA1* and *BRCA2* genes."
- cDNA is not a "product of nature" and is patent eligible under 35 U.S.C. 101

Mayo v. Prometheus
Subject Matter Eligibility of Processes

US 6,355,623 Claim 1:

„A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:

(a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointesti-nal disorder; and

(b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointesti-nal disorder,

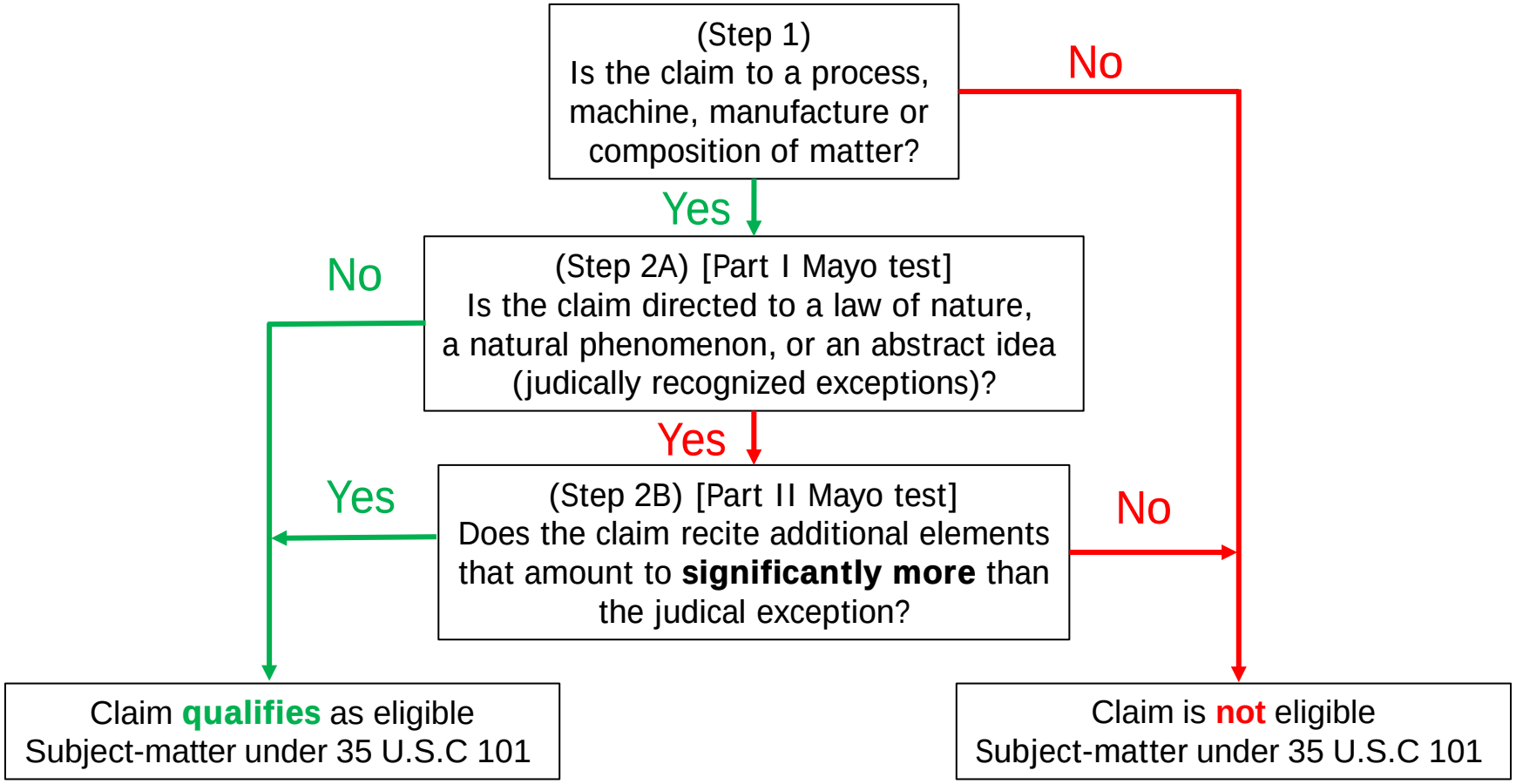
wherein the level of 6-thioguanine less than about 230 pmol per 8×10^8 red blood cells indicates a need to increase the amount of said drug subsequently admin-istered to said subject and

wherein the level of 6-thioguanine greater than about 400 pmol per 8×10^8 red blood cells indicates a need to decrease the amount of said drug subsequently ad- ministered to said subject.“

Mayo v. Prometheus
Subject Matter Eligibility of Processes

- The court found that medical tests that rely on correlations between drug dosages and treatment are not eligible for patent protection.
- The court reasoned that natural laws themselves may not be patented, and natural laws cannot be patented in connection with processes that involve “well-understood, routine, conventional activity.”

USPTO Interim Guidance on Subject Matter Eligibility



Proteins

1. Antibiotic L. ➔ Non Eligible
2. The Antibiotic L of claim 1, which is in a tetrahedral crystal form. ➔ Eligible
3. The Antibiotic L of claim 1, which is expressed by recombinant yeast. ➔ Eligible
4. A purified antibiotic comprising an amino acid sequence that has at least 90% identity to SEQ ID NO: 2 and contains at least one substitution modification relative to SEQ ID NO: 2. ➔ Eligible

Nucleic Acids

1. Isolated nucleic acid comprising SEQ ID NO: 1. ➔ Non Eligible
2. Isolated nucleic acid comprising a sequence that has at least 90% identity to SEQ ID NO: 1 and contains at least one substitution modification relative to SEQ ID NO: 1. ➔ Eligible
3. The isolated nucleic acid of claim 1, further comprising a fluorescent label attached to the nucleic acid. ➔ Eligible
4. A vector comprising the nucleic acid of claim 1 and a heterologous nucleic acid sequence. ➔ Eligible

Antibodies

1. An antibody to Protein S. ➔ Non Eligible
2. The antibody of claim 1, wherein the antibody is a human antibody. ➔ Eligible
3. The antibody of claim 1, wherein the antibody is a murine antibody comprising complementarity determining region (CDR) sequences set forth as SEQ ID NOs: 7-12. ➔ Eligible
4. The antibody of claim 1, wherein the antibody is a chimeric or humanized antibody. ➔ Eligible
5. The antibody of claim 1, wherein the antibody comprises a variant Fc domain. ➔ Eligible

Highlights from the USPTO Interim Guidance on Subject Matter Eligibility

- Includes all claims (product and process) “directed to” a judicial exception
- Step 2A analysis: compare product or process in the claim to its naturally occurring counterpart to identify ***markedly different*** characteristics (MDC)
  - Includes structure, **function**, and/or other characteristics
- Step 2B analysis: determine if additional elements alone or in combination add ***significantly more*** to the exception
- Streamlined eligibility analysis: if self-evident that claim does not seek to pre-empt all uses of the exception ➔ there are many known alternative ways to use the exception
- The mere possibility that something exists in nature does not bar eligibility

Patent eligibile claims for personalized medicine post Myriad and Mayo?

The Court's analysis of patent eligibility in *Myriad* focused on whether products occurred in nature.

- Include claims to compositions that are not naturally occurring.
  - Capture molecules (Abs/Nucleic acids) fused to a substrate.
  - Polynucleotides comprising a detectable moiety.
  - Humanized or chimeric antibodies.

The Court's analysis of patent eligibility in *Mayo* focused on laws of nature, mental steps, and routine conventional activity.

- Include claims to diagnostic methods featuring patentable compositions (e.g., antibodies, microarrays, detectable polynucleotide probes that hybridize to SNPs).
- Claims to companion diagnostics (e.g., a method of treating a patient by administering drug X, wherein the patient is selected as having disease Y).

Dr. Jörk Zwicker

Patentanwälte | PartG mbB
Radlkoferstr. 2
81373 Munich
Germany
T +49 89 998479 6
F +49 89 998479 79
E zwicker@zsp-ip.de