Diagnostic Tools for Response to 6-Thiopurine Therapy

Tech ID: 23121 / UC Case 2012-642-0

SUMMARY

UCLA researchers have developed genetic and cytometric tests to predict patient responsiveness to 6-thiopurine therapy for autoimmune and inflammatory diseases. This technology has the potential to reduce the incidence of the serious adverse effects associated with 6-TP treatment, by averting its use in patients unlikely to benefit from 6-thiopurine therapy.

BACKGROUND

Thiopurine drugs – including 6-thioguanine, 6-mercaptopurine, and azathioprine – are used to treat transplant rejection, hematological malignancies, as well as a number of chronic autoimmune inflammatory conditions. In particular, thiopurine therapy has a long-standing, proven efficacy for the treatment of inflammatory bowel disease (IBD). However, thiopurines have well-known toxic, adverse effects, which can become life threatening. These adverse effects include liver toxicity, pancreatitis, and myelosuppression, which may lead to dangerous infections. Recent insight into the pharmacology and mechanisms of action of thiopurines has led to an emphasis on dosage optimization to improve therapeutic efficacy and mitigate the risk of adverse affects. Although this approach may improve responsiveness in some patients, a significant proportion of patients that are refractory to thiopurine treatment will still be exposed to the drugs and receive little or no therapeutic benefit. In addition, dose-independent toxic effects and wide interindividual variance in thiopurine tolerance should exclude some patients from continued therapy. **Thus, a major therapeutic challenge exists in identifying which individuals will benefit from thiopurine therapy prior to administration**. New tests to classify patients as candidates for 6-thiopurine therapy would improve patient safety and outcome as well as improve utilization of clinical resources.

INNOVATION

Dr. Jonathan Braun and colleagues in the Department of Pathology and Laboratory Medicine at UCLA have devised genetic and cell-based tests to classify high- and low-likelihood responders to 6-thiopurine therapy. The technology has been founded on laboratory research exploring the genetic and immunological profiles associated with 6-thiopurine sensitivity. The tests could be performed through standard genetic analysis and/or confirmed by cellular readouts for a point-of-care setting.

APPLICATIONS

- Identifying 6-TP candidate patients for autoimmune diseases:
- Inflammatory bowel disease (IBD): Crohn’s disease and ulcerative colitis
- Other chronic inflammatory syndromes: multiple sclerosis, rheumatoid arthritis, and Type 1 diabetes

ADVANTAGES

- The tests are the first to predict 6-TP treatment efficacy based on individual genetic information
- The tests are also the first to relate genetic-based immunological traits to 6-TP treatment efficacy
- The tests require minimally invasive sample collection from blood
- The genetic assay uses methods amenable to standard high-throughput detection and simple analytic algorithm
- The flow cytometric assay utilizes available markers an d standard lab-based platforms

STATE OF DEVELOPMENT

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INVENTORS

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OTHER INFORMATION

KEYWORDS

6-thioguanine, 6-mercaptopurine, azathioprine, autoimmune disease, inflammatory bowel disease, Crohn’s disease, ulcerative colitis, thiopurine, hematological cancers, leukemia, lymphoma, myeloma, transplants, transplant rejection, inflammatory disease, inflammation

CATEGORIZED AS

- **Medical**
  - Diagnostics
  - Disease: Autoimmune and Inflammation
  - Disease: Digestive System

RELATED CASES

2012-642-0

Genetic-based immunological traits used to predict 6-TP responsiveness has been established in Crohn's disease cohort, and validated in an independent multiple sclerosis cohort, as well as healthy individuals. A retrospective genetic study with a large dataset of patients with known 6-TP responsiveness is underway. A study of the cytometric markers and their correlation to responsiveness to 6-TP in humans is currently being designed.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	10,385,395	08/20/2019	2012-642

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