NCDDGs—The First NIH Public-Private Partnerships

Created in 1982 by the NCI Board of Scientific Counselors, Division of Cancer Treatment & Diagnosis, the NCDDG Program has been adopted by four other NIH institutes. The NCDDG Program aims to:

- Support multidisciplinary team research to discover new targeted anticancer therapies.
- Address the need for new therapies with greater selectivity.
- Use new technologies to speed discovery (e.g., molecular targets, compounds libraries, high throughput screening, imaging).
- Protect intellectual property.
- Foster high-risk, translational research with potential high payoff.

NCDDG Public-Private Partnerships Work

Win, Win, Win Relationship

Government (Provides Funds and Assistance)

- Win: New treatments.

Academia (Provides Concepts and Expertise)

- Win: Access to new ideas and talent for increased competitiveness.

Industry (Provides Technology and Development)

- Win: Risk sharing and access to new ideas without the cost of increased competitiveness.

Benefits and Costs: 1984 (First Awards) to 2004

Benefits

- Discovery: 42 funded NCDDGs (diverses approaches to drug discovery).
- Development: 12 developed to clinical trial (includes 1 fast-track).
- Delivery: 4 marketed agents (3 first-in-class).

Costs

- Overall grant support (highly leveraged): About $203 million ($50 million per marketed agent).
- FY 2004 cost: $12 million (about 6% of DTP’s grant portfolio).

NCDDG Results: Four Marketed Agents

Topotecan: Example of Roles of Academic-NCI-Industry Partnership

Principal Investigator: Larry Lue, Johns Hopkins University.

Overview

- Dr. Liu discovered that DNA Topoisomerase I is a molecular target in the 1980s.
- NCI supported Monroe Wall and Mansaah Wani, Research Triangle Institute, to isolate camptothecin on contract. Sandoz camptothecin failed in NCI trials in the 1970s. NCI provided camptothecin to an NCDDG at the University of Florida in the 1980s and supported phase II clinical trials of topotecan in the 1990s.
- SmithKline Beecham produced a semi-synthetic, water soluble derivative and supported formulation, toxicology, production, and phase I clinical trials.
- Topotecan was manufactured by SmithKline Beecham as Hycamtin®. Sales were $203.5 million in 2003.

BCNU for Brain Tumors

Principal Investigators: Henry Brunn, Johns Hopkins University; Robert Langer, Massachusetts Institute of Technology.

Overview

- Dime-sized wafers release BCNU over 2–3 weeks. It is the only FDA-approved implant of its kind.
- BCNU increased median survival in recurrent glioblastoma from 11.6 to 13.9 months.
- Licensed to Gliadel®. It is the only FDA-approved recombining, chimeric monoclonal antibody against the extra-cellular domain of the human epidermal growth factor receptor EGFR, HER1, c-ErbB-1.
- A DTP contractor chimerized monoclonal antibody with the permission of the originator.
- Combined with interleukin, cetuximab yields a 23% response rate with a median response duration of 5.7 months.
- DTP and Intricema Systems signed an MTA for development of Eribulin®.

Diphteria Toxin-IL2 Fusion Protein DAB-IL2 (Dendronics Dithix)

Principal Investigator: John R. Murphy, Boston University Hospital.

Overview

- Model Three-Dimensional Structure of Diphteria-Toxin: IL2 Fusion Protein DAB-IL2, IL2 Active.
- It is licensed to NCDDG corporate partner Dendron Corporation.
- It is now seeing significant responses in a phase II clinical trial for advanced prostate cancer (FDA fast-track status).

Overview

- Objectives: Kill the leukemic cell.
- Challenge: Replace native diphtheria toxin (DT) receptor binding domain with IL-2—the ligand for the IL-2 receptor (RD2).
- Concept: IL-2 receptor is overexpressed in leukemic cells.
- Agent: Diphtheria toxin—a potent inhibitor of protein synthesis.
- Approved for cutaneous T-cell lymphoma.
- Under development for chronic lymphocytic leukemia.
- Licensed to and marketed by Ligand Pharmaceuticals, Inc. as Ontak®.

Cetuximab

Principal Investigator: John Mendelsohn, University of Texas, M.D. Anderson Cancer Center.

Overview

- Cetuximab is the only FDA-approved recombinant, chimeric monoclonal antibody against the extra-cellular domain of the human epidermal growth factor receptor EGFR, HER1, c-ErbB-1.
- A DTP contractor chimerized monoclonal antibody with the permission of the originator.
- Combined with interleukin, cetuximab yields a 23% response rate with a median response duration of 5.7 months.
- DTP and Intricema Systems signed an MTA for development of Eribulin®.

New Agents in Clinical Trials

Provenge® (NCI 720379): A Prostate Cancer Vaccine

Principal Investigator: Dr. Ronald Levy, Stanford University.

Overview

- Provenge® is a cancer vaccine based on prostatic acid phosphatase.
- It is licensed to NCDDG corporate partner Dendron Corporation.
- It is now seeing significant responses in a phase II clinical trial for advanced prostate cancer (FDA fast-track status).

Lessons Learned

- Good science is not sufficient.
- Industry is an asset—it increases speed of development but can be market-driven and risk-averse.
- Production of clinical-grade products can be rate-limiting.
- Projects are long-term investments. Payoff often comes after grant is over.
- Activities are time-intensive for NCI staff.