Alliance of Glycobiologists for Cancer Research

Manual of Operations

Version 4.0

Revision History

Version	Date	Change
1.0	8-14-07	Created Sections 1, 2, and 3
2.0	10/24/07	Revision 1
2.1	11/23/07	Revised after first teleconference
2.2	11/27/07	Revised after comments from BH and KK
2.3	1/22/08	Revised after discussion during December conference call
2.4	1/31/08	Section on Collaborative Resource Funds revised
2.5	5/28/08	Sections 3.1.3 and 3.1.6 revised on CR Funds priorities and review process
3.0	9/12/12	Revised to accommodate changes with second funding phase
4.0	2/3/20	Revised to accommodate changes with third funding phase

Table of Contents - The Alliance Manual of Operations

SECTION 1 ORGANIZATION AND DEVELOPMENT

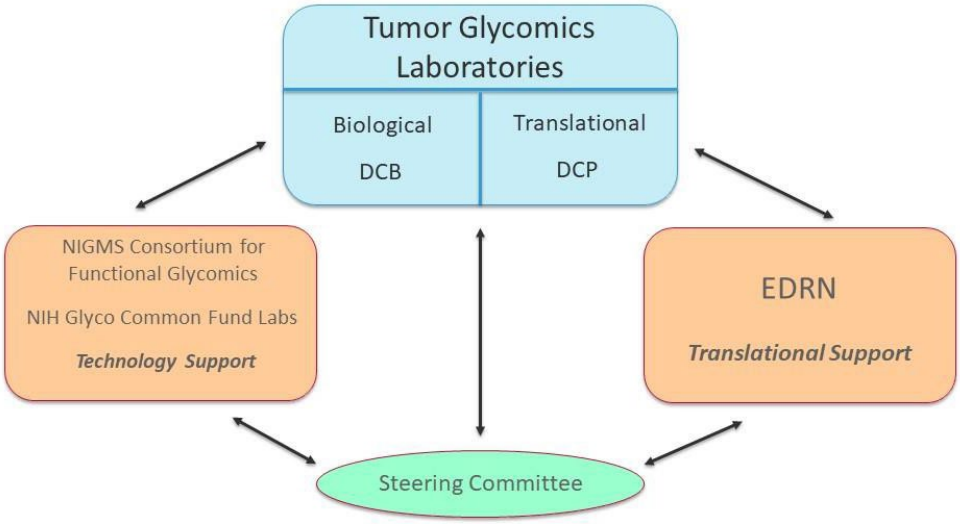
The Division of Cancer Prevention and the Division of Cancer Biology in the National Cancer Institute created the Alliance of Glycobiologists for Cancer Research (the Alliance) for supporting investigator-initiated, collaborative research the study the glycobiological mechanisms that drive cancer initiation and progression and to discover glycomic-based biomarkers for cancer detection and risk assessment. The Alliance may also be denoted the Alliance of Tumor Glycomics Laboratories. A number of NCI programmatic review groups recommended that funding for this consortium be established to support developments in this underexploited field of cancer research and translational development.

The Alliance includes three components to facilitate discovery, development and validation of cancer biomarkers:

- **Tumor Glycomics Laboratories** – These laboratories form the core component of the Alliance. They are responsible for studies in glycobiological cancer research for the discovery, characterization and development of new or refinement of existing glycan-based biomarkers. In response to PAR-17-206 or PAR17-207 each tumor glycomics laboratory assembled the necessary team to complete the research plan proposed in their respective applications.

- **Programs supported by other institutes:** The Common Fund Glycoscience Program is supported by the NIH Office of Strategic Coordination with the goal to create new resources, tools, and methods to make the study of glycans more accessible to the broader research community. The investigators of the Alliance can work with those of this program to avail themselves to the new technologies developed in order to facilitate their Alliance research. The Consortium for Functional Glycomics (CFG) was funded and is continually supported by the National Institute for General Medical Sciences (NIGMS) and are available to provide specialized reagents, services, and technology requirements for the unique needs of the tumor glycomics laboratories analyzing complex carbohydrate structures.

- **The Early Detection Research Network (EDRN)** – Funded by the NCI, the chief mission of EDRN is to promote advancement of biomarkers for early detection, diagnosis, or risk of cancer through clinical validation. The EDRN will participate with the Alliance to facilitate clinical validation of biomarkers developed by the Tumor Glycomics Laboratories. This unique collaboration should minimize the time necessary to see translation of diagnostic tests for clinical application.



The Alliance is governed by the Steering Committee, consisting of the Principal Investigators of the Tumor Glycomics Laboratories and NIH Program Staff from NCI, and NIGMS.

These procedures provide guidance for the administrative and operational activities of the Alliance and may be modified or revised by approval of the Steering Committee as experience and need dictates. Any member in good standing (i.e., a member who attends at least one Steering Committee meeting per year) may propose amendments to the procedures.

1.1 Statement of Objectives

- To support and facilitate a broad spectrum of research activities that identify cancer-related abnormalities associated with glycans and glycoconjugates that play important roles in cancer initiation or progression. Understanding the mechanisms by which altered glycosylation influences cancer initiation, progression and response of tumor cells to therapy will advance progress of translational applications for cancer prevention, detection and diagnosis. These research activities will involve a progression typified by: (a) the use of a variety of platforms and technologies for discovery of specific glycans or characteristics of glycan profiles that correlate with defined cancers; (b) a better understanding of the mechanisms by which altered glycan profiles enable tumors to proliferate, change their adhesive properties, become invasive, promote angiogenesis and suppress immune response; (c) the performance evaluation in terms of sensitivity and specificity of these biomarker candidates in case versus control clinical specimens; and (d) culmination in translational efforts to test the most promising biomarker candidates in clinical validation studies.
- To place a priority on biomarkers for early detection and primary prevention of cancer, however, markers for diagnostic clinical testing of cancer or stratification of cancer risk also fulfill the mission of the Alliance. It is possible that markers for prognosis or prediction of response to therapy may arise from this research, and where appropriate, these additional biomarker applications may be explored.
- To function as a highly collaborative consortium promoting research on the molecular roles of glycobiology in cancer. Collaboration will be fostered through open discussion of research developments and discussions of strategies to most efficiently interrogate complex carbohydrates of clinical significance.
- To contribute to the development of glycan structural databases maintained by the Consortium for Functional Glycomics (CFG) and in the Common Fund Glycoscience Program.
- To promote collaboration and communication with other relevant programs at the NCI, other Institutes within NIH, and academic and industrial leaders where the research interests coincide with the mission of the Alliance.

SECTION 2 STEERING COMMITTEE

2.1 Overview

The Steering Committee (SC) has major scientific management, oversight, and responsibility for developing and implementing a collaborative research program within the Alliance. The Committee consists of a Chair, Co-Chair, the Principal Investigators of the Tumor Glycomics Laboratories, and Program Coordinators from NCI and NIGMS.

The Steering Committee will be responsible for: i) encouraging collaboration among projects examining altered glycosylation of tumor cells and coordinating Alliance activities; ii) identifying areas of opportunity to advance current understanding of mechanism(s) by which glycan modification(s) alter cellular signaling to enhance tumor initiation and progression, that can be carried out as a collaborative project within the Alliance. Members of the SC keep updated of all projects in the Alliance through monthly conference calls and Steering Committee meetings, provide advice as needed to the PIs as projects progress, For the specific activities of the translational tumor glycomic labs the SC will offer recommendations on strategies to expedite biomarker progression to validation status, determine when specific biomarker studies are ready for larger scale clinical validation, and monitor study results of these validation studies as they progress.

The SC members also determine the rules by which the Alliance will govern itself, appropriate use of Collaborative Resource Funds for defined purposes, and propose collaborations with external scientists whose research interest or technology platforms are in line with the mission of the Alliance. Each Principal Investigator and the NCI Program Officer has one vote. The remaining SC participants act as *ex officio* members and provide valuable guidance concerning issues involving their areas of responsibility.

According to the requirements of the Cooperative Agreement, each Principal Investigator (PI) should attend the annual SC business meeting and one scientific workshop each year. In cases where the Principal Investigator cannot attend a SC meeting at least one representative from that Cooperative Agreement must be present. Additional meetings may be called as needed. The time and site for SC business meetings are determined by SC members. The minutes of the SC meetings are prepared by a specified party as a matter of record and distributed to the members of the SC for approval at the next meeting. NCI reserves the right to terminate a grant for failure to attend or have representation at SC meetings. Each PI may use her/his discretion in choosing to attend a scientific workshop covering the topics of glycobiology or biomarkers (such as EDRN-sponsored workshops).

Every PI will serve as a voting member of the Steering Committee, will attend the initial Planning Meeting for the Alliance, and will attend subsequent SC meetings or specify a senior investigator to represent the Tumor Glycomics Laboratory. The SC will also convene by conference calls throughout the year on a schedule to be decided by consensus and majority vote by the SC. The attendance of the PI at SC meetings and at least two-thirds of the scheduled conference calls is considered an essential part of the Cooperative Agreement award. Applicants must budget for travel and per diem expenses for SC meetings. In the first year, applicants should plan for the Principal Investigator to attend the Planning Meeting, SC meeting It may be beneficial for each lab/team to have a second person the first meeting

as well. In the second and subsequent years, applicants should plan for the PI or senior investigator to attend the SC meeting and one workshop per year.

SC conference calls are vital to keep abreast of recent developments within the Alliance, provide opportunities for sharing of ideas, strategizing experimental approaches for biomarker discovery, and allows time to address administrative responsibilities of the Alliance such as approvals to spend Collaborative Resource Funds. All coinvestigators from the Tumor Glycomics Laboratories may attend conference calls. Scientists from outside the Alliance can be invited to attend individual conference calls as agreed upon by a majority of the SC. For each conference call every Tumor Glycomics Laboratory must be represented by at least one attendee, and PIs are required to attend a minimum of two-thirds of these calls.

2.2 Responsibilities and Privileges

- Develop guidelines for operation of the Alliance.
- Coordinate the research program and foster collaboration within the Alliance by establishing or refining policies and procedures for collaborative projects, protocols, and Alliance-defined projects.
- Develop criteria for reviewing progress of the Alliance and establish policies for reviewing changes in projects not showing translational significance at the request of the laboratories/centers.
- Establish and track realistic milestones.
- Develop and implement rules for sharing data and resources.
- Establish procedures for submission of requests and policies for allocations of Collaborative Resource Funds.
- Develop criteria for including external scientists to participate with in Alliance activities and establishing policies for them to request Collaborative Resource Funds.
- Develop “decision criteria” for promoting promising biomarkers for clinical validation studies and determine their clinical utility such as testing early detection markers, or as risk factors.
- Develop and approve protocols to be followed in validation studies.

2.3 Chairs

The Chair and Co-Chair are elected by the full SC. Any member of the SC can offer nominations for the Chair and Co-Chair. The term of office for the Chair and Co-Chair is five years with eligibility for re-election for one additional term (for a total of 10 yrs) if funding of the Alliance is continued for another round. The Chair and Co-Chair will, if possible, alternate yearly the primary Chair duties.

2.3.1. Duties of the Chair

- Preside at all meetings of the full SC when present.

- Appoint ad-hoc committees as needed or recommended by the SC and designate special assignments within these groups as needed.
- Invite consultants as needed for particular Alliance activities.
- Prepare the agenda for SC meetings with assistance from NIH program staff.

2.3.2. Duties of the Co-Chair

- Serve as acting Chair at SC meetings/conference calls where the Chair is absent. The Co-Chair will assume the primary duties of the Chair on alternate years (years 2 and 4).

2.4 Quorum

For holding meetings, including conference calls, a quorum is defined as the presence of the majority of SC members. If a quorum is not present, voting on any issues cannot occur.

2.5 Rules of Conducting Meetings

Robert's Rules of Order will govern the conduct of meetings of the Alliance

SECTION 3 POLICIES AND PROCEDURES

3.1 Funds

3.1.1. Definitions

There are two sources of additional funds available to the Alliance investigators: Collaborative Resource Funds and EDRN Core Funds.

EDRN Core Funds can only be used for supporting validation studies of biomarkers developed by Tumor Glycomics Laboratories. Application and access to these funds is described in the EDRN Manual of Operations.

Collaborative Resource Funds (CR Funds) are provided through set-aside funds built into each U01 award. These funds are reserved for various post-award necessities of the Alliance.

3.1.2. Use of Collaborative Resource Funds

CR Funds are reserved for special needs that may arise from the unique technologies required to research complex carbohydrates and other special opportunities that may present themselves to the Alliance. These include:

- CR Funds can be allocated for the development of special resources needed by the Alliance (for example, to enhance the resource capabilities through use of technologies developed in the Common Fund Glycoscience Program).

- CR Funds may support data analysis by the Data Management and Coordinating Center of EDRN and any meeting logistical support provided by an appointed group.

- CR Funds can be used to advance or expand the proposed research objectives of the Alliance by subsidizing the procurement of reagents, services, or other resources offered by the Alliance partnering programs or other third parties.

- CR Funds may support intra-Alliance collaborative research projects that will enhance the advancement of individual or collaborative research Aims.

- CR Funds may support “pilot projects” that would focus on evaluating an interesting finding or reagent, such as an antibody or lectin, that appears to be of important interest to the Alliance.

- CR Funds may be used to supplement ongoing research of an investigator outside the Alliance who is willing to share their technology platform or advance their biomarkers provided that the focus of this collaboration meets the objectives of the Alliance

- CR Funds may support collection of clinical specimens for use by the Alliance for studies that extend beyond those proposed in their original applications.

3.1.3. Requirements for Requesting Collaborative Resource Funds

The request for CR Funds must be single-spaced and follow NIH Format, as used in PHS Form 398. It should be organized and submitted as follows:

1. Title Page (page 1 of the PHS Form 398). Description (Abstract), Performance Site(s) including the site providing the required resources/services.
2. Scientific Proposal (3 to 5 pages; 3 is the recommended length), organized into different sections depending on the category for which CR Funds are being requested.
    A. Tumor Glycomics Laboratory special needs - Rationale, Background details on the need or use of services/resources to be covered by CR Funds, any Preliminary Data (optional, if applicable), Experimental Design describing how the requested services/resources will contribute to the research plan of the applicant Tumor Glycomics Laboratory. In the case of a collaboration between Alliance Laboratories, specific details will be included that describe the roles and responsibility of each Laboratory and budget allocations (see below) to each Laboratory. One investigator will be designated P.I. and be responsible for the research described in the request. In the case of a request from the CFG or NCRR Center, the P.I. of the resource can apply directly for SC funds, denoting the benefits of reagents or services to specific Laboratories.
    B. External Investigator or Pilot Project- Rationale, Background of the proposed platform or biomarker to be investigated in conjunction with the Alliance, Preliminary Data, Technologic Design and Approaches describing how the Alliance will benefit in the development of new cancer biomarkers.
    C. Clinical Specimens - Rationale, Background describing the need for specific specimens, Preliminary Data (if applicable), Technologic Design and Approaches describing the numbers of specimens (cases & controls) required, discussion of statistical power to be derived from these numbers, and clinical criteria for inclusion in the study.
3. Budget Page - (final page unless an Appendix section is included). Use page 4 of the PHS Form 398. Adequate budget justification for direct costs is required.
4. Appendix (optional).
5. One electronic copy (in PDF form) of the proposal should be submitted to the NCI Alliance Program Office.

All projects must comply with institutional regulations on research involving human subjects, children, minority groups, gender, animals, recombinant DNA, and hazardous materials. Appropriate approvals from the relevant committees, including approval from institutional review boards, must be submitted to the NCI Alliance Program Office before funds can be provided for successful applications.

3.1.4. Review Criteria

Review criteria for CR Funds are based on the following principles, as relevant, for the different request categories described above:

- Well-defined needs of one or more laboratories in the Alliance requiring CFG, NCRR Glycomics or Glycotechnology Center support, or for a collaborative project.

- Scientific merit, potential to develop new biomarkers, or potential to significantly facilitate development of biomarkers under study, and compatibility with Alliance objectives.

- Justification of the use to commit CR Funds for the requested purpose.

3.1.6 Review Process

The entire SC will obtain a copy of every proposal. The NCI Program Director will then choose primary and secondary reviewers from among the PIs and co-PIs of the Tumor Glycomics Laboratories. An NCI or possibly other NIH program director will also be assigned to the review panel of a proposal. For any proposal with expertise outside that currently in the Alliance an external *ad hoc* reviewer can be brought in on the panel. The identities of the review panel will be kept anonymous to the rest of the CU. Each member of the review panel for a proposal will independently review the proposal before the panel convenes via conference call to discuss the proposal and arrive at a consensus. A brief summary of the panel's assessment of the proposal will be written by the primary reviewer and submitted to the NCI Program Director who will then forward this statement to the Program Review Committee (PRC).

The PRC will be comprised of three program directors from NCI, the representative program director from NIGMS, and the representative program director from NCRR. The PRC will consider the consensus statement from the review panel of each proposal, the availability of CR Funds, and the priority for funding before submitting their recommendation to NCI Program for funding.

Recommendations by the PRC may be in four categories: 1) Not recommended for funding; 2) Resubmission of a revised proposal requested; 3) Conditional approval (where relatively minor changes or clarifications are requested for NCI Program to approve funding); 4) Recommended for funding. The entire SC will be informed of all proposals approved for funding and the Chair's institution will be notified to develop a contract through the NCI Office of Grants Administration.

3.2. Confidentiality

The Alliance will be considered as "one" laboratory using "one electronic notebook" for all Alliance-supported efforts – so unless the public is invited – the SC meetings, including phone or video conferences, are considered 'lab meetings." All data (including that which has not yet been made public) are available through the electronic notebook to members of the Alliance and must be held confidential by all members of the Alliance until it is published or filed for patent. Confidentiality extends to data shared via non-public areas of the Alliance website. A blanket Confidentiality Disclosure Agreement will be signed by the respective institution(s) of each Tumor Glycomics Laboratory to cover all meetings of the

Alliance and any participation within EDRN meetings. If a non-member of the Alliance is to participate in a meeting of the Alliance, including phone and video conferences, a non-disclosure agreement must be signed by the participant(s) in advance of the meeting if confidential information from Alliance investigators will be disclosed.