

Licensing Contact: Chekesha S. Clingman, Ph.D.; 301/435-5018; clingmac@mail.nih.gov

Collaborative Research Opportunity: The NIBIB/IR/Positron Emission Tomography Radiochemistry Group and the NIAID Biostatistic Research Branch are seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize a Fluorine-18 radiolabeled analog of tenofovir. Please contact Peter Moy (NIBIB); 301/496-9270; moype@mail.nih.gov for more information.

Dated: September 17, 2007.

Steven M. Ferguson,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. E7-18798 Filed 9-21-07; 8:45 am]

BILLING CODE 4140-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Heart, Lung and Blood Institute; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The contract proposals and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the contracted proposals, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Heart, Lung, and Blood Institute Special Emphasis Panel; Heart Study Research Project.

Date: October 18, 2007.

Time: 9 a.m. to 1 p.m.

Agenda: To review and evaluate contract proposals.

Place: Hilton Crystal City, 2399 Jefferson Davis Hwy, Arlington, VA 22202.

Contact Person: Holly Patton, PhD, Scientific Review Administrator, Review Branch/DERA, National Heart, Lung, and Blood Institute, 6701 Rockledge Drive, Room 7188, Bethesda, MD 20892-7924, 301-435-0280, pattonh@nhlbi.nih.gov.

(Catalogue of Federal Domestic Assistance Program Nos. 93.233, National Center for

Sleep Disorders Research; 93.837, Heart and Vascular Diseases Research; 93.838, Lung Diseases Research; 93.839, Blood Diseases and Resources Research, National Institutes of Health, HSS)

Dated: September 17, 2007.

Jennifer Spaeth,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 07-4708 Filed 09-21-07; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Allergy and Infectious Diseases; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meetings.

The meetings will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute of Allergy and Infectious Diseases Special Emphasis Panel; Asthma and Allergic Diseases Cooperative Research Centers.

Date: October 16-18, 2007.

Time: 8 a.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: Gaithersburg Marriott Washingtonian Center, 9751 Washingtonian Boulevard, Gaithersburg, MD 20878.

Contact Person: Quirijn Vos, PhD, Scientific Review Administrator, Scientific Review Program, Division of Extramural Activities, NIAID/NIH/DHHS, 6700B Rockledge Drive, MSC 7616, Bethesda, MD 20892, (301) 451-2666, qv@niaid.nih.gov.

Name of Committee: Microbiology, Infectious Diseases and AIDS Initial Review Group; Microbiology and Infectious Diseases B Subcommittee.

Date: October 17, 2007.

Time: 8 a.m. to 6 p.m.

Agenda: To review and evaluate grant applications.

Place: North Bethesda Marriott, 5701 Marinelli Road, Bethesda, MD 20852.

Contact Person: Gary S. Madonna, PhD, Scientific Review Administrator, Scientific Review Program, Division of Extramural Activities, National Institutes of Health/ NIAID, 6700B Rockledge Drive, MSC 7616,

Bethesda, MD 20892, (301) 496-3528, gm12w@nih.gov.

Name of Committee: National Institute of Allergy and Infectious Diseases Special Emphasis Panel; Virology Program Project Application.

Date: October 18, 2007.

Time: 9 a.m. to 12 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, Rockledge 6700, 6700B Rockledge Drive, 1202, Bethesda, MD 20817 (Telephone Conference Call).

Contact Person: Gary S. Madonna, PhD, Scientific Review Administrator, Scientific Review Program, Division of Extramural Activities, National Institutes of Health/ NIAID, 6700B Rockledge Drive, Bethesda, MD 20892, (301) 496-3528, gm12w@nih.gov. (Catalogue of Federal Domestic Assistance Program Nos. 93.855, Allergy Immunology, and Transplantation Research; 93.856, Microbiology and Infectious Diseases Research, National Institutes of Health, HHS)

Dated: September 17, 2007.

Jennifer Spaeth,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 07-4710 Filed 9-21-07; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Public Teleconference Regarding Licensing and Collaborative Research Opportunities for: Novel Ligands for Diagnostic Imaging and Radioimmunotherapy; Dr. Martin Brechbiel et al. (NCI)

AGENCY: National Institutes of Health, Public Health Service, HHS.

ACTION: Notice

Technology Summary

The technology describes the composition of several 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) and diethylenetriaminepentaacetic acid (DTPA) compounds, their synthesis, metal complexes, conjugates, and their application in diagnostic imaging and radioimmunotherapy.

Technology Description

Monoclonal antibodies (mAbs) have been employed as targeting biomolecules for the delivery of radionuclides into tumor cells in radioimmunotherapy (RIT). Numerous clinical trials have been performed to validate this modality of cancer therapy.

While one critical variable that influences the effectiveness of RIT is the choice of the radionuclide and its

associated emission characteristics, an equally important aspect is the choice of the chemical means by which the radionuclide is bound to the protein. For RIT applications, radioisotopes such as ^{90}Y (Yttrium-90) or ^{177}Lu (Lutetium-177) must be linked as a metal complex to a monoclonal antibody (mAb) or immunoprotein via a suitable bifunctional chelating agent, wherein that complex must be thermodynamically and kinetically stable to minimize release of the isotope in order to minimize toxicity *in vivo*. Compounds that can easily conjugate as metal complexes, and are stable to an extent *in vivo* are needed for new imaging diagnostics and radiotherapy technologies.

In general, DOTA conjugated to mAbs display relatively slow and inefficient radiolabeling with Y(III) isotopes under mild conditions. This is contrary to the rapid and high-yield radiolabeling (>90%) of mAbs conjugated with bifunctional derivatives of the acyclic chelating agent DTPA.

Since the release of the radiometal from the chelate is a potential source of radiotoxic effects to non-tumor cells and normal tissue, a chelate that forms a kinetically inert complex with the radiometal is critical for successful targeted radiotherapy. Additionally, compounds having complex stability comparable to that of DOTA and complexation kinetics characteristics of DTPA are desirable for effective conjugation and *in vivo* efficacy.

This technology family describes the synthesis of several DOTA and DTPA based compounds. The technology family consists of three different types of compounds: (1) Backbone-substituted DOTA compounds, metal complexes, and conjugates (2) two protected variants of the 2-(4-isothiocyanatobenzyl)-6-methyldiethylenetriamine pentaacetic acid (1B4M-DTPA), (3) a protected active ester variant of the CHX-A" DTPA and (4) Substituted 1,4,7-triazacyclononane-N,N',N"-triacetic acid (NOTA) compounds with a pendant donor amino group, metal complexes, having the properties of both DOTA and DTPA.

More specifically, the NOTA compounds are substituted 1,4,7-triazacyclononane-N,N',N"-triacetic acid compounds with a pendant donor amino group. These compounds possess the same octadentate coordinating groups as DOTA and DTPA; however, these compounds have a combined macrocyclic and acyclic character. The macrocyclic component chosen is based upon 1,4,7-triazacyclononane-N,N',N"-triacetic acid ("NOTA"), while the

acyclic component is a pendant bis(carboxymethyl)amino donor group that is connected by an alkylene bridge that is optionally substituted with an aralkyl group. The cooperative binding of the pendant donor groups coupled with the pre-organization and macrocyclic effect of the NOTA sub-structure accelerates complexation with metal ions and isotopes (e.g., Y(III), Gd(III)) while maintaining a high level of stability of the complexes.

The 1B4M-DTPA and the CHX-A" molecules were synthesized for the following uses: (1) Use in the introduction of the chelator to the N-terminus of peptides, aptamers, PNA, wherein deprotection or cleavage from resin or solid phase support of the product is possible and (2) introduction of the chelator to macromolecular structures such as dendrimer wherein this is accomplished in organic solvents eliminating the gross inefficiency of the prior aqueous methods.

The compounds described in the present technology have several applications. All the compounds are useful in the conjugation of nearly all peptides, and antibodies for targeting antigens/peptides associated with cancers. Additionally, the compounds are useful for modification of macromolecules such as dendrimer, carbon tubes, etc., for labeling with radioactive metal ions suitable for imaging and/or therapy and paramagnetics for magnetic resonance imaging (MRI).

Competitive Advantage of Our Technology

It is estimated that the demand for medical imaging products will expand 3.9 percent annually to \$15 billion in 2010. The market for contrast media, radiopharmaceuticals, and other consumables and accessories will total \$4.6 billion in 2010. Radiopharmaceuticals will provide the best growth opportunities as advances in biotechnology and nanotechnology expand the availability of safe and effective compounds and extend the range of diseases and disorders that can be studied through nuclear medicine. Additionally, the market of the contrast reagents and media used in radiopharmaceuticals will also see a rise in demand.

Our technologies have several advantages over the existing reagents used as contrast agents and in metal complexes. (1) The chemistry is very flexible and provides the basis for an extensive list of conjugation functional groups to be introduced; (2) The elimination of aqueous chemistry steps in synthesizing the 1B4M-DTPA

molecules obviates the possibilities of contamination by spurious metals that could compromise subsequent radiolabeling; (3) Furthermore, the elimination of aqueous steps aids in the introduction of paramagnetic ions such as Gd(III) for MRI applications. (4) The DOTA derivatives are very stable *in vivo*; (5) The NOTA derivatives have improved stability, and faster kinetics of conjugation than either DOTA or DTPA; and (6) The general synthesis process provides a procedure for preparing dendrimer-based MR agents with higher yields and efficiency while enhancing versatility.

Patent Estate

This technology consists of the following patents and patent applications:

1. U.S. Patent Application Serial No. 10/525,673 filed April 18, 2005, entitled "Backbone-Substituted Bifunctional DOTA Ligands, Complexes And Compositions Thereof, And Methods Of Using Same" [pub.# 20060165600];

2. U.S. Patent Serial No. 7,163,935 issued January 16, 2007 entitled "Scorpionate-Like Pendant Macrocyclic Ligands, Complexes And Compositions Thereof, And Methods Of Using Same";

3. U.S. Patent Serial No. 7,081,452 issued July 25, 2006 entitled "Scorpionate-Like Pendant Macrocyclic Ligands, Complexes And Compositions Thereof, And Methods Of Using Same"; and

4. U.S. Provisional Patent Application 60/864,503 filed November 06, 2006 entitled "Method Of Preparing Macromolecular Contrast Agents And Uses Thereof".

5. PCT/US2005/028125 filed August 9, 2005 entitled "Metal Chelators And Methods Of Their Use".

Next Step: Teleconference

There will be a teleconference where the principal investigator will explain this technology. Licensing and collaborative research opportunities will also be discussed. If you are interested in participating in this teleconference please call or e-mail Mojdeh Bahar; (301) 435-2950; baharm@mail.nih.gov. OTT will then e-mail you the date, time and number for the teleconference.

Dated: September 14, 2007.

Steven M. Ferguson,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

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