May 2, 2008 Updated "one-pager" to DEDC

Group Name: Toxicology of Heavy Metals (THM) in Degenerative Diseases (DD) using NORM progeny as probes with a high resolution, high sensitivity, low background Whole Body Counter (WBC)

Science

Objectives - Studies in Toxicology, Internal Medicine, and neuro-molecular biology with a high-resolution high sensitivity Whole Body Counter (WBC) located underground at DUSEL, Lead, SD.

1. Develop a WBC spectroscopic method using gamma rays from radon progeny for whole body counting to demonstrate proof-of-concept for the real time uptake of heavy metal ions for invivo toxicological studies.
2. Optimize the WBC spectroscopic method for invivo studies to determine Pb, Bi, Po and other heavy metal ion concentrations in different organs of the Body for diagnostic purposes in cancer studies without the need for biopsy samples.
3. Apply the method to investigate correlations identified in earlier investigations with biopsy samples of brain tissues to validate the method for studies in pathology, nephrology, neuromolecularbiology.
4. Interface with researchers in pathology and nephrology to extend the knowledge base regarding the triggers for developing degenerative diseases like Alzheimer's Disease, Parkinson's Disease, and Multiple Sclerosis, and sclerosis and fibrosis in kidney tissues.
5. Refine the Toxicological knowledge base with various researchers studying neuromolecular diseases.

(pending agreements)

Approach - List of subproposal topics

For Objective 1: (Principals and Tentative collaborators)

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1. Design and build one pixel WBC using a high resolution low energy photon detector for Cranial monitoring (PI, PJ, GIL)
2. Investigate counting times and sensitivities for qualitative detection of 46 keV from 210Pb in the cranium (PJ, GIL)
3. Investigate interferences limiting counting sensitivities for applications in nephrology (NP, PJ, GIL)
4. Establish design goals for WBC instrumentation for all the vital organs in the body (GIL, BM, SG? DS? NP, PI, PJ)
5. Investigate Proof-of-concept (poc) for qualitative determination of 210Pb in the cranium by iterating steps 2 and 3. (PI, PJ, GIL, NP, SG)
6. Draw conclusions for designing multipixel WBC for studies

in nephrology, pathology, toxicology and neuromolecular biology. (NP, SG, BM, GIL, PJ, PI)

For Objective 2: (Principals and Tentative collaborators)
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1. Investigate calibration of the WBC spectroscopic method for quantitative determination of Po, Pb, Bi in the vital organs of the body for diagnostic purposes in nephrology, pathology, toxicology and neuromolecular biology. (GIL, PJ, PI, NP, BM, ?SG?, ?DS?)
2. Investigate sensitivity of the method for routine investigations in nephrology, toxicology, and neuromolecular biology (GIL, BM, SG, NP)
3. Identify issues arising in routine diagnostic applications of WBC methodology developed in steps 1 and 2 in nephrology, pathology, toxicology, and neuromolecular biology. (GIL, BM, PJ, PI, PN, SG, SC)

How the list is amalgamated into a program to address the objectives

Our program is based on an interdisciplinary integration of the expertise gained by the principals and collaborators from earlier studies over a period of more than 25 years.

We have listed above the series of investigations and experiments identified for integrating in a logical manner the expertise of the individual researchers for achieving the science objectives. The series of steps are listed in the order in which they are needed for a logical amalgamation of the steps to achieve the science goals.

It can be seen from the steps listed for objectives 1 and 2, that we need a high resolution high sensitivity whole body counter capable of in-vivo measurements in real-time as opposed to expensive and time consuming biopsy sample that have to be collected for the science across the various disciplines.

The time lines and bench marks

1. 1st half year 1: Objective - Project start up underground site selection
   shielding design
   system components acquisition
   site preparation
   personnel recruitment

2. 2nd half year 1: Objective - Assemble 1 pixel WBC
   Training of personnel and team members
   Assembly of one pixel WBC system
   Energy Calibration for cranium studies
   Preliminary test runs

Evidence for proof of qualitative sensitivity for cranium studies

3. 1st half year 2: Objective - Expansion of WBC to 2 pixels
   Assembly of pixel for kidney studies
   Iteration 2 of steps in 2 above
   Evaluation of data for qualitative diagnostics
   WBC Design Analysis and observations 1

4. 2nd half year 2: Objective - multipixel Expansion of WBC
   Negotiations based on observations 1
   Assembly of additional pixels
   Iteration 3 of steps in 2 above
   Evaluation of multipixel data for qualitative diagnostics
   WBC Design Analysis and observations 2

5. 1st half year 3: Objective - Quality assurance tests
   Negotiations for Q/A of diagnostic tests
   Implementation and Quality control tests
   Science analysis and observations 3

6. 2nd half year 3: Objective - Identifying user issues

   Science analysis and plans for year 4
   Funding proposals for years 4 and 5

7. Years 4 and 5: Objective - Technology transfer
   Discussions with medical diagnostics groups for the WBC technology transfer with the required detection sensitivity

Expected results:

1. Well tested instrumentation and methodology for medical diagnostics in nephrology, pathology, toxicology, and neuromolecular biology.
2. Synergy with interdisciplinary groups in internal medicine, toxicology, and neuromolecular biology is expected to produce need for technology transfer.

Brief description of first suite of experiments

1. **One pixel WBC Calibration for Cranium and Kidney studies**
   A one-pixel whole body counter (WBC) consists of one large area high-resolution low-energy gamma-ray detector with the required shielding for the detector to accommodate the whole body of a human. Setting up of such a device involves the determination of the ambient radioactivity in the rocks at the selected location underground, designing the required shielded cavity

around the detector, calibration of the system for the determination of the activities of interest and identification of the interferences from the ambient air-borne radioactivity.

The objectives for this experiment are: 1. To assemble a one pixel WBC with the required sensitivity to detect the NORM progeny in healthy humans without degenerative diseases; 2. To establish the operational requirements for the supply of "radon-free" air to the underground laboratory; and 3. To calibrate the WBC for the quantitative determination of the radioactivity of interest arising from NORM progeny in the human body at ambient radon concentrations in air.

2. **Study of a Candidate with multiple degenerative diseases from Lead, SD**
   As part of E&O about our project, our group established cross-cutting sessions with local population. Our focus was on the education of the population about the need to establish a WBC at the DUSEL. In these sessions our members collected anecdotal evidence for the incidence of degenerative diseases in the local population. They identified a candidate for testing Lykken's hypothesis that the NORM progeny are responsible for the incidence of degenerative diseases. A local candidate was identified and consent obtained for the testing.

   Objectives for this initial experiment are: 1. To detect the level of the NORM progeny in a candidate with multiple degenerative diseases with the one pixel WBC; 2. To collect direct corroborative evidence for Lykken's hypothesis without the use of biopsy samples in candidates with degenerative diseases; 3. To identify if the sensitivity of the WBC is adequate

3. **Study of a Control Candidate without degenerative diseases**
   The objective of this study is to collect experimental data for from a control candidate for experiment #2 above.

Development needs prior to conducting experiments at Homestake

Infrastructure engineering and design:

Radon-free air supply
Liquid nitrogen supply
Clean room systems and protocols for entry into the WBC Facility

Laboratory experiments, theoretical analyses:

Custom designed electronics and software
Monte Carlo simulation capability with MCNP
for solid angle determinations,
for shielding design and quantitative
determination of low levels of radioactivity

Cost Estimate

S-4 proposal cost **In preparation**

ISE Project cost **In preparation**

Tasks required to refine cost estimate

1. obtain latest quotes for materials and components
2. determine labor costs if human resources local to Lead, SD are used

Schedule

Estimated time required
Sequence of tasks
(start with S-4 activities) **In preparation**

Facilities required to successfully conduct experiment **In preparation**

Space
Access
Power
Equipment
Communications
Services
Special materials

Your point of contact for issues regarding facilities

Glenn I Lykken <glenn_lykken@und.nodak.edu>

E&O Epidemiological studies of degenerative studies
Relationship of NORM and progeny to degenerative diseases
non-invasive in-vivo diagnostics development

Risk identification and management

Potential problems that could affect successful outcome

Potential problems that could affect other experiments or facility

Interested principals and collaborators

Glenn I Lykken	WBC design and applications spokesperson
Ila	Spectroscopy Methodology spokesperson
Jagam	Instrumentation consultant
Berislav Momcilovic	Medical toxicology spokesperson
Don Sens	Biochemistry, Molecular biology

Scott Garrett	Molecular toxicology spokesperson
Seema Somji	Molecular toxicology, pathology
Neelaprasad	Nephrology, Physiology, Biochemistry
Lucian Wielopolski	Medical Physics, Monte Carlo modeling, Nuclear Electronics
Thomas Ward	Nuclear Chemistry, Environmental Science
P. Leela	Economics of Radon in Public Health
H. Sandstead	Nutrition and Trace Elements