The RIKEN Center for Molecular Imaging Science
December 16-17, 2008 in Kobe

Advisory Council 2008: Dr Noboru Yumoto, Prof. Koichi Tanaka, Prof. Hideo Saji, Prof. Norihiro Sadato, Prof. Mats Bergström, Dr Joanna Fowler, Prof. Bengt Långström Chairman.
Background: After Dr Doi's presentation by giving an overview of RIKEN on Monday evening the 15th of December, we had with the White book and then followed a 2 day AC-meeting starting with a more detailed review of the RIKEN CMIS by Prof Watanabe. That was followed by the 4 Research Progress reports and 1 short Research Affiliation report. All of the presentations were followed quite interesting and intensive Q&A sessions.

In summary. The AC felt that the there is a significant potential and strength in the chemistry and the design of the facility with an excellent preclinical facility especially with its access to unique in vivo models.
The AC were also impressed by the enthusiasm and knowledge of the young staff and we believe that they will be able to contribute and should have responsibility to be part in the preparation of a road map for the CMIS journey into the future.

The AC's internal discussion:
The discussion was based on the white book, the presentations and focused on the following 4 statements / questions.

1) Are there achievements with major scientific significance or achievements with significant societal impact?
2) How does the Center compare with similar research institutions abroad? Make recommendations for possible improvements based on this investigation.
3) Evaluate the Center's collaboration within RIKEN and with outside institutions, and evaluate the Center's efforts to promote international collaborations.
4) Suggest for future CMIS recruitment of research staff.

In summary referring to these 4 points the AC concluded that it was indeed difficult to evaluate and have a clear opinion on what the major scientific significance or achievements of CMIS have been and its impact on the society.

The AC decided that it will not make a detailed evaluation since the CMIS only had been in operation for 2 months and therefore we felt inappropriate to make a scientific evaluation of the CMIS performance.

However during our discussion we have proposed to Prof Watanabe to make a "Vision statement" for CMIS which could be used to give both a public and an internal view of its mission.
That statement and a Road map with milestones, timelines and deliveries would be beneficial for CMIS mission and would be valuable for the future evaluation of its achievements.
We asked Prof. Watanabe to produce such material and it is attached to the report.

The AC discussed has structured the report using a SWOT strategy (Strengths, Weaknesses, Opportunities and Threats).
The input on this analysis was based on the information we have gained in advance and during the presentations and discussions during the meeting.

As a general statement we would like to say that the CMIS facility is outstanding and that the facility and the personal has a tremendous potential with a number of strengths but we also can see that there is a need of focusing.

That is why the AC felt that CMIS and RIKEN would benefit of a Vision statement and road maps would be valuable for the future so that the visibility of the research strategy will be clear.
The AC had a long discussion about the statement of CMIS that there is an intention to be involved in "drug development".

We would like to moderate that wording and instead put in a perspective of aiming to explore and develop Molecular Imaging techniques which can have an impact on the future the drug development. So the focus should mainly be to develop MI tools for specific targets of interest in science in general, in drug development and in potential diagnostic application.

We would also like CMIS to prioritize some specific biological targets which both has a scientific value and might have an impact on society.

<u>Strengths</u>
The strong chemistry will have an impact on labeling chemistry for the future development of Molecular Imaging (MI).

Labeling chemistry is an essential component of in vivo MI technology. The strong basic chemistry is an essential component of the competence of CMIS. Future plan for the advancement of this competence should be reinforced in the "roadmap".

Very excellent research animal facility and especially having access to both anesthetized and non anesthesia primates and rodents for system biology is a unique asset and should be kept strong.

The advantage of having access to non-anesthetized PET study for PK (pharmacokinetic) /PD (pharmacodynamic) study is evident. With careful preparation and treatment of the animals and dedicated machinery setup, the established animal PET measuring system for both anesthetized and non anesthesia primates and rodents (White paper P34-39) is a unique asset for studies of system biology.

To belong to a strong research organization like RIKEN is very valuable, since it may link and have early access to new exciting future science.

To belong to RIKEN is an important strength for CMIS, because **MI research is in "an interdisciplinary field that melds various branches of research, including synthetic chemistry, nuclear chemistry, biochemistry, applied physics, molecular biology, cell physiology, pharmacology, clinical medicine, mechanical engineering, electrical engineering and computer engineering"** (White paper P3).

Within RIKEN, collaborations with the advanced science institute like Center for Developmental Biology, Brain Science Institute, SPring-8 Center, Bio Resource Center, Systems and Structural Biology Center, and Research Center for Allergy and Immunology have already been launched and should be given high attention(White paper P61).

RIKEN covers the majority of these fields except for clinical medicine. CMIS is, however, placed in a medical cluster in KOBE, enabling close and mutual collaboration with the clinical medicine. Collaboration with Institute of Biomedical Research and Innovation (IBRI) regarding translational research is an example (White paper P61). **This link with medical cluster in KOBE makes CMIS unique among the research centers of RIKEN**.

Potential scientific heights

Based on these strengths of the institute, the energetic and enthusiastic researchers, CMIS is expected to accomplish high level scientific achievement on international level. Some projects are challenging like development of specific cellular MI in pancreatic

beta-cells, cancer stem cells, peri-neuronal progenitor cell, and lymphocyte subset imaging. These projects include development of MI probes for abundant molecular recognition to specific nucleic acids, glyco-conjugates, proteins, and peptides in the life science and may enable CMIS to become a center of excellence in MI.

Weaknesses

If the drug development is what CMIS claims, the pharma perspective regarding clinical trials 2-4 is missing and that needs substantial resources

As the drug development is a long and complex process, certainly one research institute of CMIS size cannot cover the entire process. Thus, it is essential to clarify which portion of the process the CMIS could or like to contribute to, particularly in relation to the pharmaceutical companies which handle clinical trials 2-4.

To end translational research with phase 0 phase 1 clinical trials in man is missing.

One of the contributions of CMIS to drug development could be to speed-up the decision process in drug development and support “to proceed or quit” question.

CMIS is under resourced for the "planned missions" (alternatively needs focusing to get visibility)

It is thus essential to clarify which portion of the process the CMIS could contribute to.

Lack of some depth in biological targets.

Limited resource (such as human and time) might be concentrated in order to achieve high level scientific achievements.

Opportunity

Use chemistry and animal for PK/PD bringing new knowledge to the field.

Allowing full PK/PD modeling if Phase 0-1 human studies is becoming available.

New scientific MI tools to facilitate the introduction of new drugs into the practice of health care.

The in house competence could contribute to the early phases of the drug development, i.e. selection of the leads.

This could be achieved by the combination of labeling chemistry, animal models and PET imaging systems that CMIS has established.

Through research collaboration with pharma there is a possibility to have access to knowledge and molecules.

Need of a balanced attitude towards pharmaceutical companies is important.

Collaboration with several research institutes has already been planned and should be developed (Whitepaper, P61).

RIKEN / CMIS has no formal responsibility to educate: **however CMIS could be a leader in the mission of (fostering) especially regulatory bodies regarding safety/risk benefit analysis.** This is a key point for the future of MI and will have a positive societal impact. CMIS should also be aiming for international collaborations. Bring in people with a deeper understanding to some areas of human physiology and who can bring in questions around the clinical need.

The combination of labeling chemistry and PET imaging systems is a powerful combination to explore physiology and patho-physiology and this is an area where high level scientific achievement by CMIS and their collaborators can contribute significantly.

Use the strengths to get visibility by high class publications

High class scientific publication is the best way to get visibility, at least better than patent.

Threats

Overestimating CMIS's capability to develop drugs

Not able to clarify which are the main areas where CMIS should contribute to.

If emphasis is on the production of patents, that may distract from high profile publications.

Sub-critical resources may drive CMIS to become a service organization to pharma (need a well planned road map).

Missing to inform researchers in- and outside CMIS about the directions of the research conducted because of the interdisciplinary functions CMIS.

Internal mechanisms to keep a self critical attitude should be clarified.

Clear and eminent research target with significant societal impact should be made visible. We would like as an example to see chronic fatigue syndrome previously and continuously investigated by Dr Watanabe et al.to be such a target to on a road map.