

Neuroscience Institute Cavalieri Ottolenghi (NICO) Peer Review 2015

The signatories have been appointed by the Board of Trustees of the Fondazione Cavalieri Ottolenghi as external experts to evaluate the performance of the scientists working at the Neuroscience Institute Cavalieri Ottolenghi (NICO), Turin, 5 years after the initiation of its activity in 2010.

- Paula Marques Alves is CEO of the IBET, Instituto de Biologia Experimental e Tecnologica, Oeiras, Portugal. She has longstanding experience in biotechnology.
- Marina Bentivoglio is full professor of Histology at the University of Verona and a renowned expert in the brain connectome and neurobiology of disease.
- Marco Celio is full professor at the Department of Medicine of the University of Fribourg, Switzerland and specialized in structural and system neuroscience.

The Panel of external reviewers visited NICO on January 28 and 29, 2016. This report has been compiled partly on Friday, January 29, at the NICO, and partly by e-mail exchange in the days following the visit. It reflects the opinion of the three members of the Panel.

General

Before the site visit, the Panel members received a detailed **internal report of the 5 year activity of NICO**. The report presented the NICO organization and outreach activities, listed the seminars held at the Institute by invited speakers, and contained “auto-evaluation forms” of each laboratory. These forms presented the laboratory personnel, the principal investigator (PI)’s CV and 5 year (2010-2015) publications, the publications of other group members, the past research activity and future plans. This NICO internal report was very well organized and complete, and the Panel members have greatly appreciated it. It was very helpful for an insight in the Institute and its evaluation.

During the site visit, the Panel members were kindly assisted by the Director, Alessandro Vercelli, and by the coordinator of the NICO Scientific Committee, Marco Damietto. The Panel members had the opportunity to attend, in a relaxed and pleasant atmosphere, the presentations of the PIs, to discuss with the Director and the groups working at NICO, and to visit the Institute. The scientific presentation of each laboratory, made by the PI, was followed by private interviews, first with the PI and then, individually, with two or three junior group members previously selected by the NICO governance for the interview. The Panel members also discussed informally with the PIs on the occasion of two dinners.

All the interviewed persons had very positive comments (upon explicit request during the private interviews) on the **NICO Director**, Alessandro Vercelli, stating that he is very supportive and devoted to his task. It was obvious that the sudden and

premature demise of the first NICO director, Ferdinando Rossi, was perceived by NICO scientists as a shocking loss, and that they were all grateful to Alessandro Vercelli, appointed in 2014, for his empathic and efficient leadership.

Strengths of NICO

An inspiring environment. Throughout the 2 days of the site visit, the Panel members could feel a harmonic atmosphere permeating the Institute. During the private interviews, all the personnel of each group (the PIs and his/her coworkers), pointed out the lack of conflicts in the Institute and the good and collaborative atmosphere reigning within each group, as well as between groups.

The success of the “shared facilities” and “being together” formula. Both senior and junior investigators stated that the NICO format of sharing common laboratory spaces and equipment had turned out being very stimulating from both the theoretical (instigating new collaborative projects and common publications) and practical (exchange of know-how and techniques) points of view.

It was clear to the Panel that the sharing of facilities is a positive aspect of this community. The “working together” had created an “*esprit de corps*” and, as a consequence, pride to belong to NICO. All the PIs used the same NICO-template as a slide-background, stressing their affiliation to the Institute. The general intention of making the name of NICO nationally and internationally prestigious transpired during the presentations and discussions.

The symbiosis under the same roof of basic neuroscience research groups from the University of Turin, engaged in various fields of research, and clinical expertise (the Clinical Neurobiology Laboratory, led by Antonio Bertolotto, from the San Luigi Hospital in Orbassano) is a unique and stimulating feature of NICO organization.

Qualified PIs. The PIs, most having spent part of their curriculum in foreign labs, gave professional presentations of interesting projects, at the research front in competitive areas, with numerous ongoing national and international collaborations.

Bright and dedicated junior scientists. The Panel members were very pleased to remark the presence of bright, enthusiastic junior scientists in all groups. They replied candidly, without any shyness or arrogance, to the questions during the private interviews. Although all worried for their careers and future positions, they all expressed confidence in the respective PI, and enthusiasm for their affiliation to NICO.

State-of-the art equipment. During the visit to the laboratories, the Panel members could appreciate the presence of state-of-the-art equipment for almost all subfields of neuroscience, installed adequately in modern facilities.

Weaknesses at NICO

A number of issues were also raised.

Problems common to the Italian context

Research funding. All the PIs complained about the fact that raising money for research is becoming a «*tour de force*» for scientists in Italy. The lack of funds undermines creativity and amputates the ranks of the research groups. Given the paucity of national funds and national calls for grant applications, funds should be raised at international level, in highly competitive calls. Information on the different possibilities offered by funding agencies, professional help to fully exploit the possibilities of European Commission and European Research Council calls are badly needed by Italian neuroscientists, and NICO is no exception.

Experiments using animals. The introduction of the new animal experimentation-law in Europe is linked to various unknown, which will probably complicate the work of those working with rodents in general, and with genetically modified mice in particular.

Perspectives in the career of junior scientists. The precariousness of many positions, particularly at the lower level of the academic scale makes many collaborators anxious.

To this general Italian issue, the problem of the proof of independence of junior scientists is added. A number of competitive grants for junior investigators require now evidence of capability of independent research. This is especially difficult in Italy, given that the senior investigator in general has the funds, and is responsible for planning the research accordingly. Given the current international situation, measures should be envisaged to foster anyhow independent work by junior investigators. In a reality like NICO, such delicate issue could and should be openly discussed.

Specific issues at NICO

- The common **office space** for the PhD-students and postdocs is appreciated, but its limitedness and crowding has been repeatedly pointed out during the interviews. Despite solidarity and friendship in the daily work, all young team members criticized the lack of office space, in particular for the difficulty of studying and concentrating.
- The problem of the **scarcity of technicians**, persons in charge of routine techniques and responsible for maintaining their continuity, was also repeatedly raised during the interviews. Technical help would save time and enhance productivity.
- **Some pieces of equipment** (e.g. in the electrophysiology Unit) are still state of the art but not “*à la pointe*”. It is mandatory to renew the technical equipment to

increase efficacy of research and the acceptance of results in the scientific community

- The problem of the **distance from the center of Turin** has been raised by the professor involved in teaching at the University and by other members of NICO personnel. However, the burden of commuting does not seem a deterrent for the professors to be present on site as long as possible to direct and counsel their collaborators. Furthermore, maintaining an association with the University is crucial for recruiting the brightest students as collaborators.
- The Panel noticed a preponderance of female junior scientists. This may reflect the general trend of an increased female representation in higher education. For scientific endeavors, a balanced gender representation would probably benefit creativity.

Research at NICO

- All PIs come from excellent schools and have a solid scientific background in neuroscience.
- Most of the PIs work in very competitive fields (stem cells, neurodegenerative diseases) but there are groups active in niche field (e.g. neuroendocrinology) or groups that have acquired a dominant position in their field (e.g. multiple sclerosis research).
- The PIs are not immune to the general tendency of overstating the importance of their work for translational (clinical) applications. The Panel cautions to promise goals that cannot be attained and to convey with precaution the translational potential of data.
- The results of the research work are published almost exclusively in international, peer-reviewed scientific journals of good to very-good renown and impact.
- The Panel members welcome the creation of a **spin-off** to commercialize the knowledge of the members of the NICO-scientific community. This activity may lead to the generation of funds that could be reinvested in research.

The NICO laboratories *(listed in the order of presentation during the site visit)*

Brain development and disease (PI Alessandro Vercelli)

- This is a very competent and highly productive laboratory. The “multitasking” PI, endowed with uncommon energy and initiative, has good relationships with his coworkers and multiple national and international collaborations.

- In terms of topics, the number of research directions could be decreased and focused on the most promising and strategically relevant for the NICO scientific mission. The laboratory name could also be less “broad” and adapted to reflect the existing key competences. This would allow for a clearer identification of the unique know-how of this lab and differentiate it, internationally. A brainstorming among the group could be done to find a new lab name.
- Access to expertise in molecular biology (at the NICO environment) would be beneficial to the laboratory, allowing the scientists to embrace even more complex and multidisciplinary projects around a core topic and maintain the excellent international network and collaborations.

Neuroendocrinology (PI Giancarlo Panzica)

- This is an excellent laboratory with a track record of solid, focused research.
- The Panel highlights the uniqueness of the key competences of this laboratory, since, at the international level, laboratories devoted to this field are not very numerous. This research topic is crucial for understanding the relationship between Man and Man-made environment, critical to provide evidence that can contribute to establish new rules and behaviors enabling healthier populations. For example, the results obtained in the last years by this laboratory at NICO could be highly relevant for European, and even extra-European, international legislation on “endocrine disruptors”.
- The “marketing” of the research of this laboratory could definitely be improved to increase grant success rate. This could highly benefit from *ad hoc* professional support and assistance (see final notes).
- In view of the PI’s retirement in a few years, adequate planning of the succession is needed to maintain high level activity in this original research field.

Neurobiology of Brain Plasticity (PI Annalisa Buffo)

- This laboratory was somehow left “orphan” by its initial leader, Ferdinando Rossi. Excellent efforts have been done by the PI, Annalisa Buffo, to finalize projects previously coordinated by Rossi. This task was accomplished and reflected in several publications by the group.
- During the last year the PI focused on the group reorganization; she should now carefully consider themes on which to focus. The name of the research group could also be more focused.
- It is worth to highlight the presence of some highly promising junior scientists who could eventually aspire to more independence.
- The laboratory has a good international network and pro-active attitude in finding funding sources (namely with industry, services via a spin-off, etc).
- Know-how on molecular biology at NICO environment could benefit even further the group outputs.

Adult Neurogenesis (PIs Luca Bonfanti and Paolo Peretto)

- The competencies of this laboratory are built on solid knowledge. The laboratory, however, works in a field which is very competitive (and “fashionable”) at the international level. Finding a niche, based on original thinking, in this field is, therefore, mandatory. The “comparative neuroanatomy” approach to adult neurogenesis is certainly solid and interesting, and should be pursued. However, this approach may not be sufficiently “hot” for fund-raising and substantial networking.
- The group is productive and seems to benefit from its double leadership, as well as from collaborations established within the NICO. Such internal networking could certainly be enhanced through further “cross-feeding”, especially in view of grant applications.
- In the NICO report, the group’s publication actually lists mostly publications authored by the PIs, so that, as in other laboratories, the independence research potential of junior coworkers requires attention.

Neuropsychopharmacology (PI Carola Eva)

- Interesting and successful research with state of the art techniques (transgenic and conditional KO mice for the *Npy1r* gene).
- The complex behavioral research in which the laboratory has embarked could account for problems in productivity in the past (e.g. in the years 2012 and 2013). If the main research line is long and demanding, side-projects able to generate additional productivity in the meantime should be envisaged.
- The laboratory has established highly qualified collaborations at the national level.
- The NICO environment and networking (e.g. collaboration with the Neuroendocrinology laboratory) could be mutually stimulating and productive.

Neurophysiology of Neurodegenerative Diseases (PI Filippo Tempia)

- This is a small group with solid expertise in modern neurophysiological techniques. The group has local and international collaborations.
- The laboratory works in a niche field (ataxia) that should remain the focus of research.
- Caution is needed in the translational approach and interpretation for the transfer of results from mice to humans.
- This group seems to be the only one with expertise in neurophysiology at NICO, and its know-how could be better exploited for internal networking.

Clinical Neurobiology (PI Antonio Bertolotto)

- The laboratory is engaged in remarkable, internationally recognized research in the field of multiple sclerosis.
- Perhaps the name of the group could be changed in “Neurobiology of Multiple Sclerosis”?
- The laboratory has obtained results relevant for the clinic and the Health Care System, namely in the challenging field of biomarkers identification for better diagnosis, development of targeted treatments and implementation of cost-effective policies, critical for Health Care systems (decision making) policies. The laboratory has a unique collection of biological probes.
- The Panel was impressed by the untapped potential in the activity of the PI, who has established a remarkable collection of blood and cerebrospinal fluid samples of multiple sclerosis patients. The PI is very active in establishing collaborations with clinicians, academics and industry being able to create partnerships and warranty continuity in obtaining research funds for his lab (through different types of funding sources).
- An association of the PI to the NICO spin-off should be promoted.
- In view of the PI’s retirement, adequate planning of his succession is needed to maintain at NICO this competence center in multiple sclerosis.

Nerve Regeneration (PI Stefano Geuna; due to health reasons, the PI was unable to attend the day of the Panel meeting and was replaced by Luisa Muratori)

- The laboratory has built up on solid knowledge, working on a challenging topic and with interesting translational applications of research results. The future projects could, however, be better defined and oriented towards the strengths of the group.
- The Panel noted a very high productivity of the PI as co-author (including publications in journal with rather low impact factor). However, only senior authorship is a key criterion for research agencies to grant funding, whereas middle authorship is useless for receiving grant support. In addition, a more selective criterion for publication could be applied, aiming at quality rather than quantity.

Final notes and suggestions of the Reviewers:

- **NICO has a very unique research environment** where scientists can share freely ideas, equipment and space.
- **Mission, vision and strategy of NICO** could be further refined and young collaborators should be involved in the development of such a vision and strategy. The size of NICO, which comprises 8 laboratories, allows common

actions, both in terms of fostering collaborations, and of a **common platform for grant applications**.

- **The PIs have an international reputation** and are supported in their endeavor by many, highly respected research workers. Strong and effective **interdisciplinary** training is given to young graduate students and post-docs. However, in general, **young researchers should be given more responsibilities**.
- **Scientific independence of junior investigators**. The reviewers suggest empowering junior researcher to publish independently from the PIs or as senior author. The international scenario currently requires proof of independence of junior investigators. **NICO could represent an example of such policy in the national reality/context**.
- **Professional support for writing grants**. To help NICO scientists in the formulation and preparation of their grants, keeping them constantly informed of public and private funding opportunities, professional help should be provided by NICO in the form of a freelance fund-raising specialist. The assistance of animal welfare officers for compiling protocols for animal experimentation could also be of help to the scientists.
- In these difficult economic times there is much **potential for NICO cooperation** in commercializing academic research and working with industry. Such goals need to be seen as enhancing the impact of research and not as a diversion. It is the task of the Director to convince NICO scientists that such cooperation can advance pure science and is essential for funding ongoing activities. **The arrangements for patent ownership and royalty sharing need to be made clear with the competent bodies of the University and with the Foundation**.
- The need to **retain and adequately-resource research workers** even in these difficult times should be further emphasized. Their retention will stimulate others to perform well. If they leave, high quality scientists may be difficult to attract back.
- The existence of a **funding scheme**, with an annual budget fully supported by the Foundation, and exclusively devoted to open, competitive international calls, with a regular basis, to distribute a limited number of **NICO Post-doc and/or PhD fellowships** and of **NICO starting project grants** to junior scientists would be beneficial and help to promote the brightest and more competitive junior investigators and raise an international environment at NICO. This would also launch the name of NICO and of the Cavalieri Ottolenghi Foundation internationally.
- The **creation of an external advisory board**, including international members, made up of independent peoples in various field of research and using different approaches is suggested.

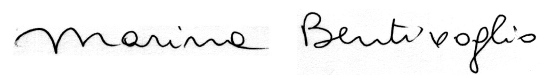
Other issues: "logistic" recommendations

- Respecting the nice architectural plan of the NICO building, private office space should be created, especially for junior investigators.
- NICO should urge on the competent authorities to ameliorate public transportation from and to the city center.

The Panel,



Paula Alves



Marina Bentivoglio



Marco Celio

February 13, 2016