

## NICO Evaluation Committee

### Report from the onsite visit, January 2020

#### Committee members:

Paolo Cassano, MD, PhD, Dept. of Psychiatry, Massachusetts General Hospital, USA

Gilberto Fisone, PhD, Chair, Dept. of Neuroscience, Karolinska Institutet, Sweden

Marco Martina, MD, PhD, Dept. of Physiology, Northwestern University, USA

Luiz Pessoa (committee chair), PhD, Director, Maryland Neuroimaging Center and Dept. of Psychology, Univ. of Maryland, College Park, USA

Angela Sirigu, PhD, Director of Research, Institute of Cognitive Science Marc Jeannerod, CNRS and University of Lyon, Lyon, France

Lucia Sivilotti, PhD, Dept. of Neuroscience, Physiology and Pharmacology, Division of Biosciences, University College London, UK

Michèle Studer, PhD, Institute of Biology Valrose, iBV, Univ. Côte d'Azur (UCA), Nice, France

Yuliya Zaytseva, MD, PhD, Dept. of Psychiatry and Medical Psychology, 3rd Faculty of Medicine, Charles University in Prague, Czech Republic

#### Summary

On January 13-14, 2020 the Evaluation Committee conducted an onsite visit and met with PIs and lab members of each research group presently active at NICO to evaluate the scientific productivity and business organization of the institute and to suggest future directions. Over these two days of discussion the committee has come up with the following conclusions and suggestions concerning the institute as a whole and the individual research groups it hosts. Overall the committee had a very positive impression of the institute, its scientific and administrative accomplishments and of the many investigators that foster its scientific productivity. All committee members were impressed by the spirit of collaboration existing between the different research groups, and by the wide spectrum of techniques and projects. It was also noted that through a well-managed shared instrumentation plan the institute maximizes the return on investment for advanced instrumentation. A few shortcomings were also noted, mostly, but not entirely, related with the overall ecosystem of scientific research in Italy. The specific points that were discussed are summarized here, starting with the general considerations and then followed by evaluations of the individual research groups.

Overall, the Institute has been very successful in establishing an excellent, collaborative research environment at the University of Turin. Outreach activities are outstanding and far exceed what is typical of Italian institutions, showing notable commitment to engage with the public and to search for non-conventional funding sources.

## Strengths

### **Environment**

The Institute provides an excellent environment in which to conduct world-class neuroscience research. From the vantage point of the committee, the nine research teams interact harmoniously with shared goals and very high dedication to brain science. The overall harmony is all the more noteworthy given that the research groups share equipment (see below) and space. The collaborative atmosphere was evident across all levels of seniority, from graduate students to full professors. Indeed, non-PI investigators very frequently highlighted how they greatly benefit from the cooperative environment at the Institute. The congenial atmosphere has led to multiple collaborations among the research groups. The collaborative spirit of the Institute, therefore, clearly exceeds that observed in larger departmental structures, and supports the cross-fertilization of ideas in a manner that has the potential to considerably enhance the quality and impact of the science conducted.

### **Equipment**

The Institute hosts excellent, shared facilities and equipment. The new equipment added in 2019 is a particular strength, including a two-photon confocal microscope. The anticipated arrival of a light sheet microscope in early 2020 is another important addition.

### **Research**

Research performed at the Institute spans from basic to clinical and translational, with both breadth and depth. Together, the research portfolio is diverse and displays complementarity across the research groups. Considerable research mentoring by senior investigators is evident across the Institute, and significantly contributes to the quality of the overall research environment. Overall, the quality of the research at the Institute varies from “very solid” to “excellent internationally”. Whereas there is some variability, no noteworthy weaknesses in particular research groups were noted.

The research at the Institute is in most cases well-funded, with an overall 53 projects active in 2019, although some teams have very low funding (see below). A further positive point is that the amount of funding request has increased substantially recently, indicating that investigators are attempting to compete for larger types of grant at national and international levels.

## Issues and recommendations

Administrative agreement. An important issue concerns the administrative status of the Institute. At present, NICO is a physical workspace that cannot be a grant-subcontract entity. Accordingly, as all research PIs are members of particular departments at the University of Turin, grants are awarded to departments that administer them. This organization creates a considerable amount of inefficiency, which impedes research progress because the Institute lacks autonomy to administer grants expeditiously. Furthermore, the current structure is a frequent source of stress to investigators at all levels. Therefore, establishing a formal agreement between the Institute and the University is urgently needed. In this respect, a grant-

overhead procedure should be implemented that guarantees the fair allocation of resources across University departments and the Institute.

Teaching load. At most research universities across the world, the teaching load is considerable. This is simply the reality of research life at academic institutions, which naturally have a teaching mission that must be met. This is understandable at the faculty level, but at the Institute the high teaching load extends to some of the postdoctoral fellows, including those on short term contracts and not tenure-track. Whereas this may be part of the structure of universities in Italy, and teaching experience may be useful in career progression, we urge the Institute to seek ways to ease this situation and at the very least to make teaching workload allocation transparent. Failure to do so is likely to have long-term impact on the future of the quality and impact of the research at NICO.

Geographical distance. The distance between NICO and other University departments is considerable and is associated with a long commute between them. Whereas this is a problem for almost all persons involved in research at the Institute, it is particularly onerous to younger students and post-docs who do not own a car. Therefore, we encourage the Institute to seek resources to establish a shuttle service between NICO and a central campus location in Turin.

Personnel. Shared administrative and technician support is available at the Institute. However, the available personnel are insufficient to meet the demands of the large corpus of investigators. Therefore, we recommend that the Institute seek funds to hire additional personnel to support its research goals.

## Other recommendations

Grant writing. Effective grant writing is an essential component of a successful research career. As noted above, senior investigators at the Institute are effective in mentoring junior investigators. However, given the competitiveness of the grant application process, we recommend that the Institute organize more structured grant-writing mentoring. A particularly effective strategy would be to create grant-writing groups with mock review panels that would provide constructive feedback.

Research scope. The scope of research at NICO is commendable. However, neuroscience is a rapidly changing field and tremendous current effort is aimed at the development and refinement of neurotechniques. Among them, activity silencing and enhancement targeting particular cell subpopulations has become a central tool in neurophysiology (e.g., optogenetics). Therefore, we encourage the Institute, as it evolves and/or expands, to consider adding research groups developing or employing such techniques, particularly in the area of physiology. This is particularly important because the latter is poorly represented at NICO.

Grant sources. We suggest that NICO investigators also consider funding from US sources. Some investigators have already sought funding from US agencies, but increased awareness of opportunities across the Institute would be valuable. Where industrial funding is obtained, a clear overhead policy should be formulated and the PI should receive advice and support in negotiating fair conditions cf. IPR and the contract costing in general.

Research groups. Naturally, research groups vary in size at NICO. Some larger groups are evidently thriving. However, the committee felt that some of the smaller groups are experiencing some difficulties as evidenced by low morale in the group. Therefore, explicit initiatives could be implemented to attempt to remedy potential problems.

PI Meetings The high level of interactivity and shared resources (core facilities, etc.) is an important asset for the Institute. To further foster the current scientific and technical cooperation it is important to implement and maintain regular meetings open to all research group leaders.

Job stability. Multiple investigators expressed concerns about job stability. The committee understands that this is tied to the academic organization in Italy but urges the Institute to seek creative ways to ameliorate this problem. Lack of minimal job stability may promote considerable “brain drain”, as more qualified investigators may seek positions outside of Italy. A better defined tenure-track program would encourage younger researchers to acquire international experience (at the doctoral or postdoctoral level) maintaining their interest and motivation to continue their academic career at NICO. There were some excellent examples of good practice in mentoring of junior researchers, with the PI encouraging and helping in submitting grant applications. Notably some PIs strove to shield the junior researchers from excessive teaching workload (at the price of their own increased teaching hours).

Staff Recruitment: It is noteworthy that NICO has recruited young investigators from other European countries and outside EU. This is an outstanding practice which is likely to bring international visibility and to enhance the diversity and creativity of NICO’s research groups. Some fellows from non-EU countries might have personal resources or be eligible for scholarship that could fund their salaries.

Visibility: NICO has done an excellent work of outreach to the public and to disseminate science in the local community and in the social media space. However, for the quality of the work conducted at NICO, it is striking that the institution is not popular among the broad scientific-neuroscience community of researchers. NICO is well-known nationally in the Italian neuroscience community. This needs to be addressed partly by targeting social media platforms followed by the international community of researchers and partly by funding young NICO researchers to allow them to present in international symposia. International scholarships for young investigators are competitive means to attend at no or limited cost international symposia.

IP Protection: Strikingly there are no incentives for NICO and for its investigators to generate IPs. This is a major loss for all, including for the university of Turin. NICO should be allowed to pursue patent applications without prior approval from the University of Turin, as long as NICO can bear all related legal costs. The University of Turin and NICO should negotiate the split share of royalties. NICO should be allowed to license IPs to the industry. This deal would be a win-win for both parts (NICO and University of Turin). It is imperative that this administrative agreement happens. This might also benefit at large the local biotech community of entrepreneurs. A balanced way of splitting the potential income of IPs is the following: 25% to University, 25% to NICO as an institution; 25% directly to the sundry funds of the labs who generated the IPs; 25% to the personal-private funds of the investors (to be split among inventors based on the extent of their contribution to the IPs).

## Individual lab reviews and recommendations

### Bertolotto group

The research group led by Dr. Antonio Bertolotto is the only clinical group at NICO and as such represents an important catalyst for collaborations. The lab specializes in diagnosis and treatment of multiple sclerosis, including the determination of the susceptibility to different drugs. Overall, the lab has achieved outstanding results. Since 2016 they have published 31 papers; Dr. Bertolotto is corresponding author in 15 of these papers. In the past years the group has taken advantage of SIMOA (single molecule array) technology, an ultrasensitive technique that detects proteins at femtomolar concentrations to study the plasma concentration of neurofilaments. The group has obtained preliminary data suggesting that this approach may become the most relevant tool to monitor axonal injury and treatment efficacy. Importantly, the preliminary data suggest that blood neurofilament may increase before any clinical symptoms, thus representing a potential game-changer for multiple sclerosis therapy. Additionally, they have created CRESM a biobank for multiple sclerosis patients that is the only biobank supported by the Italian node of BBMRI-ERIC in the Piedmont region. The biobank, which already stores data from >1000 patients, is gaining international visibility and already sent hundreds of samples around the world.

#### Strengths:

- The lab is a top clinical laboratory and has developed approaches that are potential game-changers.
- The Biobank initiative is a very worthy initiative, and is placing the lab at the center of clinical ms research in the world.
- The lab is very well funded.
- They train 2 to 3 undergraduate students/year; these students receive considerable mentoring and support

#### Weaknesses and Recommendations:

- The lab could benefit from having additional space and one technician to perform photometry. Photometry would help expand the biobank.
- The biostatistician would enormously benefit from having more computing power. A possible remedy could be obtained by purchasing access to an external server such as Cineca.
- An open question concerns the fate of the laboratory when the PI will have to retire. Although the PI is aware of the problem and is trying to address this, there is still concern that much of what is currently done in the lab is strongly dependent on the remarkable activity of the PI. The fact that the biobank is now recognized by BBMRI-ERIC gives hope that at least this very worthy initiative will keep thriving.

## **Buffo group**

The research group led by Dr. Annalisa Buffo focuses on: (1) the contribution of the glial cells in pathophysiology, promoting myelin repair and rescue of oligodendroglia pathology; (2) revealing and exploiting the mechanisms of the astrocyte plasticity and their heterogeneity in the development and (3) developing of the replacement strategies and promoting circuit restoration. The PI of the group, Prof. Dr Buffo is an internationally renowned scientist who is also a deputy director of NICO, and has various scientific roles, as a delegate of the outreach activities in the department of neuroscience of the University of Turin, a member of the research observatory of UNITO. The group has 6 members with various expertise: two assistant professors (one in tenure track), 3 postdocs and one PhD student. Each branch of the research activities is handled by 2-3 post docs and a PhD student which seems to be balanced in terms of the workloads.

In the last 3 years the group demonstrated an excellent research activity and published 14 manuscripts in high impacted journals. They contributed into the field with the novel data showing: (1) evidence that microglial extracellular vesicles act in vivo as multimodal and multi target signaling mediators affecting myelin repair and inhibiting myelin regeneration through the regulation of astrocyte reactivity; (2) the first proof of principle that allele-specific silencing strategy can treat diseases caused by gene duplications, thus opening new therapeutic opportunities for several pathological conditions linked to gene copy number gains; and (3) an excellent use of FAST (Fluorescent cell Analysis Segmentation Tool), the first fully automated method for the segmentation of stained cells and tissues labeled by multicolor combinations of fluorophores. The track for the future projects is well defined and will follow the current goals and focus also on the clinical (neurological) aspects including motor deficits, lesioned striatum etc.

### Strengths:

- Excellent funding both national and international (currently 4 active grants), not only dependent on PI activity but also brought by postdocs including international fellowships (IBRO stipend, SINS Travel grant).
- Within NICO, the group closely collaborates with five out of six research groups, has numerous international collaborations (University of Munich, Germany; University of Rochester, UK; University of Pennsylvania, USA, CRCHU de Quebec, Canada, University of Southampton, UK etc).
- All members of the group are active in the scientific and outreach research activities. Prof. Buffo has numerous invited talks (including international), science communication activities, various editorial duties including a role of the topic editor for *Current Opinion in Pharmacology* and *Frontiers in Neuroscience*. She is also a member of the Scientific Summer Academy (A.Buffo); deals with the coordination of the student exchange activity and organizes the UnistemDay (L.Bonfanti-A.Buffo). Post doc students serve as *ad-hoc* reviewers for international journals, are involved into the organization of the workshops, schools, conferences.

### Weaknesses and Recommendations:

- Since the group is dealing with many ongoing grants, the agreement with the University is essential for establishing the financial procedures.

- The group lacks a technician that could take over a laboratory job.
- Budget for the seminars (both international and national) is not sufficient.
- Given that the PI of the group deals with the students exchange activities, more students are expected to be in the lab. To date, only one PhD student is a lab member and is only co-supervised by the PI. No international students are currently based in the lab, though it might be beneficial.

### **Di Cunto group**

The research group led by Dr. Ferdinando Di Cunto has recently joined the NICO from another Institute of the University of Torino, the Department of Molecular Biotechnology and Health Sciences, and is composed of 1 post-doc, 1 PhD student and 1 Master student. The scientific focus of the PI has been for a long time understanding the genetic and non-genetic mechanisms leading to normal and/or pathological brain conditions. In particular, he has been studying for many years a neurological disorder called MCPH17 and characterized by microcephaly, intellectual disability, spasticity, axial hypotonia, and epilepsy. This syndrome is due to mutations in citron (CIT), leading to loss or inactivation of the citron kinase protein (CITK), and results in primary microcephaly in humans and rodents, associated with cytokinesis failure, asymmetric cell divisions and DNA damage.

The main objectives of the team regarding this syndrome are to understand how mutations in Citron kinase lead to microcephaly, what are the potential substrates and partners, and the molecular consequences of CITK loss in terms of defective cytokinesis, DNA damage, and microtubule destabilization. The team is also working on the role played in Down syndrome by TTC3, which is one of the candidates belonging to the Down Critical Region, and how it interacts with Citron proteins. In addition, they aim to study other non-genetic factors leading to microcephaly such as infection by the virus Zika.

The team combines different approaches, such as computational biology, biochemistry, molecular biology and experimental analysis, *in vitro* and in animal models. The PI has published several very good to excellent papers on the majority of the topics described above and obtained national and international grants. He recently obtained a grant that will allow him to use the *C. elegans* model (in collaboration with a Neapolitan team) for testing CIT human variants. More recently and considering the strong involvement of CITK in proliferation, the team has hypothesized that CITK might be involved in brain tumor cells, in particular those that characterize the pediatric tumor medulloblastoma. To this purpose, the PI managed to obtain a very consistent grant from the AIRC foundation.

#### Strengths:

- The team has a solid basic research in the field of brain neurodevelopmental diseases and has produced excellent science and publications in the recent 5 to 10 years.
- His choice to join the NICO, be in closer contact with clinical researcher and use the excellent platforms of the Institute will strengthen his research quality in neuroscience.

- . On the other hand, thanks to his deep expertise in bioinformatics, he can work on challenging questions, such as anti-correlation-based drug repositioning in Down syndrome patients, find novel targets and/or drugs and actively collaborate with several groups at NICO.
- . Overall, he has demonstrated for many years now that he can secure his research with excellent funding resources at the national but also international level.

Weaknesses and Recommendations:

- . The major weakness of this lab is the number of projects in relation to the size of the team. - The PI has only young people and the most senior one (the post-doc) plans to move abroad. - He definitely needs to recruit more postdocs and try to attract candidates for researcher positions able to secure him a critical and more stable mass of people.
- . -The PI should focus on the most promising and funded projects and leave some of them for the future when the size of the lab will increase and his people will become independent and efficient.

**Eva group**

The research group led by Dr. Carola Eva is a small group consisting of Dr. Eva, two PI (Assistant Prof level), one senior postdoc and one PhD student. At the moment, the group also includes two Master students. Past activity has been mainly centered on the study of neuropeptide Y (NPY). The laboratory has produced seminal work on this topic, including the characterization of the role of NPY-Y1 receptors in the limbic system, utilizing mice with a conditional knock out (PNAS, 2011). The laboratory has consistently followed up this initial work with additional studies published in prestigious journals, such as Biological Psychiatry (2014) and more recently Cell Reports (2019). An additional project involving Dr. Ilaria Bertocchi, one of the PI in the group, centers on the role of NMDA receptors in the oxytocin system and has led to a collaborative paper published in Neuron (2019), with another paper in preparation. Future lines of research will investigate the role of perineuronal nets in fragile X syndrome and autism spectrum disorders. This idea stems from results originally obtained studying the NPY-Y1 receptor (Bertocchi et al. *NPY-Y1 receptor signaling regulates spatial learning through modulation of perineuronal nets*. Submitted for publication). The group will also study behavioral and cognitive conditions associated with epileptic encephalopathies. In this project, the lab will use a transgenic mouse model based on overexpression of a mutated form of the GluN2A subunit of the NMDA receptor, which has been found in epileptic patients.

Strengths:

- . The laboratory has produced excellent science and publications in spite of its small size.
- . The research topics fit very well with the overall mission of NICO. Overall, solid basic research in the field of neuropsychopharmacology with good translational potential.

Weaknesses and Recommendations:

- . The main problem for this otherwise excellent group is of financial nature. Only one grant (pending) is listed and shortage of personnel represents a serious hinder to the feasibility/completion of the proposed studies.



- . An effort should be made by NICO to help the group to secure adequate support, for instance by involving its researchers in internal collaborations/networks.

### **Panzica group**

The Neuroendocrinology group led by professor Giancarlo Panzica (PI) includes an associate scientist, professor S. Gotti, (CoPi), 3 PhD fellows and two master students. Research activity in this team which involves the use of a rodent model, focuses on the role of steroid hormones in modulating brain circuits, body homeostasis and behavioral sex differences. A first topic deals with the effect of gonadal hormones in regulating hypothalamic neuronal activity and their central role in determining sex related response to diseases vulnerability. Another important topic having a societal impact is neuroendocrine dysfunction after hazard exposure. Two studies led by Gotti have shown hormone receptor interactions with chemical compounds (bisphenol A) producing endocrinal changes during the perinatal and the puberty stage or with natural isoflavones (genistein) inducing dopaminergic alterations. Also, the group is committed to extend human diseases such as anorexia nervosa into a preclinical model and recently they showed the role of maternal separation in the onset of food disorders. For their future projects, the PIs are planning to continue their studies by focusing on the role of estradiol on neuroendocrine circuits and in regulating food intake. They will also keep on tracking the link between hormones and psychiatric disorders. Research production of this group is good with a total of 8 publications for 2019. Mentoring seems also successful given the number of papers each PhD student signs as first author. Also, the PIs have obtained a good number of grants (even if a good amount come from the University of Torino), they have been active in locally organizing meetings and in participating in the Nico spin off activities.

#### Strengths

- . The question of the role of hormones on brain and developmental behavior is currently experiencing a revival in neuroscience in the context of brain/body axis investigations. Hence, this group can play a major role in the Italian and European research community.
- . The translational impact of this research is appealing, specifically in relation to psychiatry.

#### Weaknesses and Recommendations

- . The PIs should recruit postdocs and promote academic positions of young (consolidator) scientists to boost the team.
- . An effort should be made to publish in journals that have higher scientific standing.
- . The PIs should increase applications for more competitive national (MIUR) and international grants (ERC, HFSP, ESF, etc.)

### **Peretto/Bonfanti group**

The group is headed by two PIs, Drs. Paolo Peretto and Luca Bonfanti, 2 Associate Professors and 1 Assistant Professor with permanent permissions, 3 postdocs, and 4 PhD students.

The laboratory's research addresses multiple aspects of brain structural plasticity, spanning from classic adult neurogenesis to the study of "immature" neurons, focusing on questions of progenitor specification, hormone-linked mechanisms, lesion-induced repair, and mechanisms of "young neuron" reservoir. The laboratory investigates multiple types of plasticity occurring in different brain regions of different mammalian species. The approach spans molecular, cellular and functional levels. The laboratory's approach spanning from molecule to behavior, and within a comparative framework, attempts to widen the understanding of brain plasticity, with a view to developing translational models that can eventually be applied in humans.

*Strengths:*

- . The lab investigates questions surrounding neurogenesis from multiple standpoints, including a strong comparative approach
- . The conceptual and theoretical approach of the lab goes beyond classic adult neurogenesis, and is fairly unique. The lab's research has the potential to propel the study of neurogenesis and related questions in novel, important directions.

*Weaknesses and Recommendations:*

- . The research of the two PIs proceeds at times with some independence. Although such complementarity has some strengths, it also poses some challenges in terms of a lack of integration between the two subgroups. In this respect, establishing additional joint lab meetings should be beneficial.
- . The recent award of the Human Frontiers program grant is a very positive step. Nevertheless, the lab should seek additional external funds to support its research mission.
- . The publication productivity of the lab in terms of first/last authored publications is reasonably good, but on the low side given that the lab has two PIs and three other professors.

**Raimondo group**

The research group led by Dr. Stefania Raimondo, who at 42 is the youngest PI at NICO, has been in charge of this group since the previous PI, Professor Geuna, was appointed Rector of Turin University in October 2019. The group's research topic is peripheral nerve repair and regeneration. The group is very productive. As a whole, in 2016-2019 it has published 53 papers. Professor Raimondo has published 18 papers of which 5 as last author and 4 without Professor Geuna. The papers are well cited.

We met two postdocs (Fregnan and Muratori) and one Masters student (Carta). We did not meet Dr Ronchi (tenure track Assistant Professor, RTDB). Fregnan has 11 years of postdoctoral experience and has published 8 papers since 2016, one as first author, 6 with one or other or both of the PIs.

The group's research focuses on studying the basic mechanisms of peripheral nerve regeneration and on developing therapeutic strategies and repair techniques with a mix of in vivo and in vitro models. The most applied projects assessed the usefulness of conduits for nerve repair produced by decellularizing nerve allografts or from biomaterials such as chitosan,

silk or PHA. There was also a line of work attempting to reproduce in vitro the effect of stretching peripheral nerves during physical therapy in man (neurodynamic therapy).

Strengths:

- Most of the projects are well established, with clear experimental plans and aims that were convincing and coherent.
- The translational focus is extremely strong, in an area that seems close to therapeutic applications.
- Well established collaborations with industry, with as many as three companies involved.

Weaknesses and Recommendations:

- The project on neurodynamic therapy seemed less clearly formulated than the others.
- The research funded by industry has been very successful, but it appears to have been a mixed blessing. It was not clear whether contractual terms were equally advantageous for the research group and for the companies involved (eg whether the costing was realistic in terms of the work involved). The panel was told that industry funding produces very short-term contracts for the postdocs and some of the results are subject to publication restrictions for commercial reasons.
- It was not clear whether contracts included fair overheads (for NICO or the University) and a fair allocation of any monetary benefits from patents. Worse still, it appeared almost impossible to establish whether the university has benefited at all from the patents connected with the work.
- Postdocs had a substantial teaching load and one of them had been a postdoc for more than 10 years.
- This is a relatively small group that would benefit from help, for instance from access to a shared administrative clerk. It was generally felt that the University should offer greater support to a group so successful in attracting money from industry.

### **Tempia group**

The research team led by Dr. Filippo Tempia is the only electrophysiology group at Nico. The group has a strong expertise in cerebellar physiology and is now starting to work on the prefrontal cortex. Although small, the group is productive having published 14 papers since 2016. Dr. Tempia appears as the corresponding author in 4 of the papers; Dr. Hoxha, a tenure track investigator in the group is the first author on 6 of the papers.

Overall, the scientific output is solid. The most recent work concerned the characterization of FGF14, an intracellular protein controlling neuronal excitability and synaptic transmission, as an important target gene in brain disorders, including schizophrenia. This work has recently received some funding and the PI plans to further focus future effort on the prefrontal cortex.

Strengths:

- Electrophysiological expertise. As the only group with this expertise this lab plays a very important role in NICO's ecosystem, as supported by the numerous internal collaborations. Additionally, the track record in the field of cerebellar physiology is excellent.
- Translational focus. The PI has been able to combine research in basic neurophysiological processes with research on different disease models. This is expected to increase funding and collaborations.
- Collaborations. The group is very collaborative, having established fruitful collaborations both within and outside NICO.

*Weaknesses and Recommendations:*

- Funding is limited. Despite a good publication record and translational relevance of the research, funding is low, and this limits future productivity. The panel wondered whether competitiveness for funding might be improved by consolidating the scientific output into a smaller number of higher impact papers.
- Potential lack of focus. One potential risk of the many collaborations established by this group is that it may cause lack of focus. This is particularly true in the case of small labs, where pursuing side projects necessarily reduces the effort on the main research. It may be wise to focus on collaborations within NICO, and, outside of NICO, on those where the possibility to receive direct funding is the highest.
- This being a small lab, there is a heavy load of non-research related work on the lab members. The panel noted that access to a shared administrative clerk for ordering would help enormously all small labs.

**Vercelli group**

The research group led by Dr. Alessandro Vercelli is one of the largest research groups at NICO, composed of 5 PIs with positions at associate/assistant Professor level, 1 postdoctoral fellow, 3 PhD students and 2 researchers supported by fellowships. Past work covered a large number of topics ranging from neurodegenerative disorders to developmental studies. This led to an excellent scientific production, with more than 20 peer review publications produced during the last 3 years in important journals, including PNAS, Scientific Reports, Neurobiology of Disease, and Cell Death & Disease. Many of these publications are the results of collaborative studies through an impressive network of internal, national and international contacts.

The group's proficiency is further demonstrated by the high level of competitiveness in attracting external funding from prestigious sources such as the Telethon Foundation in Italy and the European Commission program Horizon2020 (with Dr. Vercelli as coordinator).

Current research lines are centered on axonal development and growth, cell death mechanisms and stem cell therapy in nervous system pathologies, including Alzheimer's and Huntington's disease, spinal muscular atrophy and spinal cord injury. Experimental approaches are based on the combined use of animal models, molecular and cellular analyses, and advanced imaging, including rodent and human MRI. The projects are a natural continuation of previous, successful

studies, often based on well-established collaborations, with a very good degree of feasibility. They are well structured and individually assigned to the PIs in the research group.

Strengths:

- . Broad scientific portfolio managed by a well-established work distribution within the research group.
- . Outstanding proficiency in securing financial support at national and international level. This will likely progress judging from the several pending or planned applications.
- . The group is active in recruiting external scientists, as in the case of Dr. Corrado Cali, who will start as PI with expertise in advanced imaging techniques (3D electron microscopy).
- . Dr. Vercelli is among the founders of PharmaFox Therapeutics AG, a startup devoted to the development of drugs against neuromuscular diseases. Some of the PIs in the research group have been involved in this work, particularly with regard to the characterization of biologicals (proteins) with potential therapeutic value.

Weaknesses and Recommendations:

- . The diversified lines of research carried out in the group might in the long run represent a challenge with regard to optimal coordination, funding and scientific productivity. The way the team is organized in terms of projects is confusing and should be improved.
- . Overall, the team should increase focus on fewer specific and most promising projects.
- . In connection to the previous point - the group is currently including several very experienced researchers. An effort should be made in the future to promote at least some of them to independent research group leaders at NICO.