7th international workshop on the CCN family of genes: Nice to be in nice

Bernard Perbal

Received: 14 June 2013 / Accepted: 14 June 2013 / Published online: 6 July 2013
© The International CCN Society 2013

Abstract In this Editorial, I would like to provide our readers with a brief mid-year update about our activities and efforts to bring together researchers working on intercellular signaling proteins at international meetings. The roots emerged about 20 years ago in the discovery of three genes originally designated *cyr61*, *ctgf*, and *nov*. The proteins encoded by these genes were first proposed to constitute a family of proteins (CCN) which now comprises 6 members (CCN1, CCN2, CCN3, CCN4-6) including the *wisp* proteins. These proteins were recognized to share a striking structural organization and a high degree of identity although they exhibited quite distinct biological properties. After historical considerations regarding the reasons for using the CCN acronym, and how the ICCNS publishing landscape that drove the ICCNS from Cell Communication and Signaling to the Journal of Cell Communication and Signaling, this short update will focus on the 7th edition of the International Workshop on the CCN family of genes to be held in Nice, Oct 16–19, 2013.

Keywords CCN proteins · CCN1 · CCN2 · CCN3 · CCN4 · CCN5 · CCN6 · *ctgf* · *cyr61* · *nov* · *wisp* · *nwCCN* · ICCNS · JCCS

Historical considerations

The CCN family of proteins and the ICCNS: When and why?

The concept of a CCN family of proteins emerged in 1993, when P. Bork (Bork 1993) proposed that the *cyr61* (cystein rich) and *nov* (nephroblastoma overexpressed) genes encoded

proteins shared a striking tetra-modular organization and a high degree of primary structure identity with a newly discovered protein called *ctgf* (connective tissue growth factor).

As discussed in a recent review (Perbal 2013), the *ctgf* and *cyr61* proteins were showing positive effects on cell growth control. While the full length *nov* protein was reported to inhibit cell proliferation, the amino-truncated version of *nov* that was cloned from a Myeloblastosis Associated Virus type 2 (MAV2-N)-induced nephroblastoma was found to induce morphological transformation of primary chicken embryo fibroblasts (CEF). Therefore, the CCN (*cyr61*, *ctgf*, *nov*) family of proteins contained positive and negative regulators of cell growth.

As it is often the case in Science, when the “fruit is ripe”, several individuals collect a similar one in their back yard...

Quickly, the collective way of thinking and the developing techniques led to the discovery (and re-discovery) of the same CCN genes, and to the description of three new members of the family, that were originally designated by the WISP acronym.

Interestingly, several variants were identified in normal and pathological conditions (Perbal 2004, 2009) and more recently, the existence of a newt-specific CCN protein was reported (Looso et al. 2012)

After discussing the matter with Herman Yeger who was very supportive to the idea, I proposed Lester Lau and Gary Grotendorst to organize a meeting on the CCN family of genes. We all agreed that there was a real need for communication, and exchange of ideas, reagents and concepts among the principal investigators who had become engaged in active CCN research.

The first international workshop on the CCN family of genes was held in Saint-Malo in 2000, and was a success thanks to the participation of leader PIs in the field, and to the outstanding local organization by Annick Perbal.

During this meeting, a group of leader PIs including L. Lau, D. Pennica, H. Yeger, P. Schofield, D. Brigstock, and

B. Perbal (✉)
International CCN Society, Paris, France
e-mail: perbalbernard@gmail.com

myself engaged in a brain storming session during a memorable dinner at a restaurant in the old city of Saint-Malo.

My proposition to create a scientific society to gather scientists working in the field and to promote communication with researchers working on other aspects of cell growth regulation was welcomed by all the colleagues who were present. A steering Committee was constituted, and a few months later, the International CCN Society, ICCNS, was born.

It is during this first CCN meeting that the participants were consulted about the pertinence of the names that had been given to the CCN proteins when they had been first discovered.

As it is often the case, genes and their encoded proteins had been assigned names that described the biological situation in which they had been originally discovered.

However, it was quickly apparent that the original names were either not appropriate or misleading.

For example, cystein-rich was not helpful in relating the *cyr61* protein to the CCN family, as many other cystein-rich proteins were known. Similarly, the overexpression of *nov* that we had reported in the avian model of the Wilms' tumors, turned out to be a choice of limited interest as our own studies indicated that the expression of the *nov* gene was not, or barely, increased in human Wilms' tumors. The third example was even more striking, as experimental evidence clearly indicated that *ctgf* was not a growth factor per se, but was acting as a co-factor in cooperation with other growth factors.

Having considered different possibilities and bearing in mind that the six CCN proteins showed very distinctive biological properties and appeared to bind to more than one receptor, it was proposed to designate these proteins with the CCN acronym that was originally coined by P. Bork, and to assign a number to each of the CCN proteins, that would indicate their order of discovery. An official proposal was put forth by the chair persons of the first CCN meeting (Brigstock et al. 2003).

Hence, *cyr61* became CCN1, *ctgf* became CCN2, *nov* CCN3 and the *Wisp* proteins became CCN4-6.

The ICCNS journals

A second major step in the organization of our group was achieved when in 2003 I created the electronic open access Cell Communication and Signaling journal at BioMed Central, that became the organ journal of the ICCNS.

After 5 years of running CCS and achieving a reasonable flux of manuscript submissions, BioMed Central decided to charge the authors for submitting manuscripts to all BMC journals. Considering that this position was not in line with our views of publishing in Science, the whole editorial board decided to resign.

Discussions were then initiated with Peter Butler who considered favourably my proposal to have the journal hosted by Springer. In order to avoid confusion with our previous publication, we decided to move on with a slightly different name and we created the Journal of Cell Communication and Signaling (JCCS), which became the new official journal of the ICCNS.

I have had the pleasure to act as the Editor in Chief of JCCS for 4 years until 2010 when I then asked Professor Andrew Leask to become the JCCS scientific Editor in Chief. Andrew has been very active in promoting JCCS and opening it up to new topics, new readers and to new submissions from outside the CCN field. Progressively, JCCS is becoming a journal devoted to the publication of articles describing the alterations of cell behaviour leading to pathological conditions.

This smooth transition is in line with our increasing knowledge of the biological properties of the CCN proteins and their implication in several key processes governing cell proliferation, differentiation and death, both in normal and pathological conditions.

In our previous publishing activity under CCS attention was not paid formally to the recognition of the Impact Factor, and thus we had to start from scratch with JCCS. However, this has now changed and recent calculations assigned an unofficial IF of 3.42 for 2011 to JCCS (see <http://springer.com/12079>). Relative to other journals this is indeed impressive and we do hope that our continuing efforts will help to maintain a high standard and scientific quality for the manuscripts published in JCCS where such recognition will translate into an even better official IF shortly.

With this as an encouragement we would be pleased to consider your work for rapid publication in JCCS, both on line and in printed issues.

Importantly, the close relationship that exists between the ICCNS and its official journal JCCS, is a vital means of leverage for enabling the communication between scientists sharing common scientific interests and goals.

As I will soon discuss in this journal, Excellence in Science requires fruitful collaborative approaches. I once wrote when I was Editor in Chief of CCS that "Communication is the Key" (Perbal 2003). Not only is it the key to scientific progress, it is also the key to universal improvement of our society's condition.

International CCN workshops on the CCN family of genes

The warmth of a family spirit is central to the goals of the ICCNS.

International CCN Workshops as Communication Means embodied in this concept aim to provide the ground for worldwide exchange of the most up to date knowledge, and for scientific education without boundaries.

What made the success of the International CCN Workshops since the year 2000, are the following points:

- i) All students and young researchers are given the same time as senior speakers for their oral talks if their contribution is of good standard. This is rather unique among the many symposia and others meetings that tend to favor and place more importance on the “invited big shots” who leave the meeting shortly after they have delivered their talks....
- ii) Each ICCNS workshop is a (CCN) family type of meeting which provides the young scientists the opportunity to interact with the senior scientists established and recognized in their field. This is also rather unique. In most meetings, these budding investigators cannot even approach the key speakers...
- iii) Everybody who pays registration fees can participate equally in the meeting, share good times with colleagues, and transmit both their passion and knowledge to the younger generation. In spite of the fact that nobody has ever been invited to the ICCNS meetings, except for the recipients of the ICCNS-Springer award (see our web site), all key leaders in the CCN fields have attended regularly the International CCN workshops, in Europe, Japan, or Canada.
- iv) Our primary goal is to educate the younger scientists, and promote collaborations not only between PIs but also, through direct contact, between established and these young scientists. This is why we pay so much attention to the time allocated for poster sessions, coffee breaks, lunches and other social activities.

All colleagues from outside the CCN field, who have attended the International CCN workshops have kept unforgettable memories that make the ICCNS spirit very unique.

II-The 7th workshop—October 16–19th 2013

We send out a warm invitation and encourage all of our readers to share unforgettable moments with us, and establish very profitable collaborations during this coming meeting. The 7th workshop will provide you with a unique opportunity to meet the key leaders in the field of CCN biology.

Registration is now open.

May we also suggest you consider becoming a member of the International society CCN?

Several alternatives are available and if you decide to become a Silver member, you will be given the opportunity to sponsor a young scientist for one of the scholarships that our Sponsor Springer provides to help young investigators to attend the CCN meetings (see <http://ccnsociety.com>)

This year, the ICCNS—Springer Award will be presented to Professor Carlo Croce (see http://ccnsociety.com/springer_award/award2013.html) who kindly accepted my invitation to give a keynote lecture on microRNAs and Cancer.

It is a great honor for the ICCNS to have Professor Croce present in Nice at the Workshop. Professor Croce has also accepted to chair a session during the meeting.

The implications of CCN proteins in fundamental biological processes (including fibrotic diseases, cancer, inflammation, developmental regulation) and their recognition as potential targets for molecular medicine, has focused a lot of attention on this family of proteins from the scientific community.

The provisional program, which is posted on the ICCNS website illustrates the high standard of the communications that will be presented by the core of the worldwide recognized leaders in the CCN field during the workshop.

On behalf of the ICCNS, I would like to take this opportunity and invite you and/or members of your laboratory to attend and actively participate in what promises to be a very special meeting!

Number 7 is claimed to be the number of perfection.
Come and join us, and “Let it be”.

Professor Bernard Perbal
June 11 th, 2013

Acknowledgments Thanks are due to all those who have made the ICCNS and JCCS what it is now. Without them, without you, the CCN field would not be. I wish to thank again my close friend and colleague Herman Yeger for his advice and editorial help.

References

- Bork P (1993) The modular architecture of a new family of growth regulators related to connective tissue growth factor. *FEBS Lett* 327:125–130
- Brigstock DR, Goldschmeding R, Katsube KI, Lam SC, Lau LF, Lyons K, Naus C, Perbal B, Riser B, Takigawa M, Yeger H (2003) Proposal for a unified CCN nomenclature. *Mol Pathol* Apr 56(2):127–8
- Looso M, Michel CS, Konzer A, Bruckskotten M, Borchardt T, Krüger M, Braun T (2012) Spiked-in pulsed in vivo labeling identifies a new member of the CCN family in regenerating newt hearts. *J Proteome Res* 11(9):4693–704. doi:10.1021/pr300521p, Epub 2012 Aug 27
- Perbal B (2003) Communication is the key. *Cell Commun Signal* 1(1):3
- Perbal B (2004) CCN proteins: Multifunctional signalling regulators. *Lancet* 363(9402):62–4, Review
- Perbal B (2009) Alternative splicing of CCN mRNAs It has been upon us. *J Cell Commun Signal* 3(2):153–7. doi:10.1007/s12079-009-0051-9, Epub 2009 Apr 28
- Perbal B. (2013) CCN proteins: A centralized communication network. *J Cell Commun Signal*. 2013 Feb 19. [Epub ahead of print]