



*Historical article*

## History of the International Collaborative Group on Hereditary NonPolyposis Colorectal Cancer

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### The beginnings

The International Collaborative Group on Hereditary NonPolyposis Colorectal Cancer (ICG-HNPCC) is 14 years old. It was conceived in Jerusalem in August 1989 during the 2nd International Conference on Gastrointestinal Cancer organized by Paul Rozen. During this meeting, Giuseppe Cristofaro of Brindisi, Italy, proposed to Henry T. Lynch (Figure 1) that they should form a group of interested colleagues throughout the world to study HNPCC and to form multiple collaborations in the interest of investigating the genetic, clinical and pathologic aspects of the disease. Henry T. Lynch, Jane Lynch, Patrick Lynch, Jukka-Pekka Mecklin, Giuseppe Cristofaro, Jim St. John and Hans Vasen then met informally and agreed that this idea was quite logical given the growing interest in HNPCC. We



*Figure 1.* Professor Henry Lynch, past Chairman and current patron, ICG-HNPCC.

reasoned that the syndrome's genotypic and phenotypic heterogeneity would require the study of large numbers of families with detailed pedigrees. These studies would involve meticulous clinical histories, molecular genetics, pathology, surveillance, and management concerns, as well as genetic counseling, in order to grasp a better understanding of the disorder and, most importantly, to benefit the high risk patients and families. Further discussion and announcement about the establishment of the ICG-HNPCC took place in November 1989 at a plenary session of an International Meeting on Colorectal Cancer sponsored by Joji Utsunomiya in Kobe, Japan (see Figure 2).

### ICG-HNPCC

In 1990, Hans Vasen, M.D., organized the first formal meeting of the ICG-HNPCC in Amsterdam, The Netherlands (see Figure 3). Thirty representatives from eight countries were present, and a report of this meeting was published in *Diseases of Colon and Rectum* [1]. It was at that time that the first Amsterdam criteria for a clinical diagnosis of HNPCC based on family



*Figure 2.* James Church (Chairman LCPG and ICG-HNPCC) dining with Hans Vasen (co-founder and Administrative Director of ICG-HNPCC) in Kobe, Japan, 1989. Photo courtesy of Hans Vasen.



Figure 3. Group photo, ICG-HNPCC meeting, Amsterdam, 1990. Photo courtesy of Hans Vasen.

history were established (see Figure 4). Meetings were subsequently held annually as follows:

- 1991 Torino, Italy, organized by Giuseppe Cristofaro
- 1992 Crete, Greece, organized by Hans Vasen
- 1993 Houston, USA, organized by Patrick Lynch
- 1994 Milan, Italy, organized by Lucio Bertario
- 1995 Helsinki, Finland, organized by J.P. Mecklin
- 1996 Buffalo, New York, USA, organized by Miguel Rodriguez-Bigas
- 1997 Noordwijk, The Netherlands, organized by Hans Vasen. This was the first combined meeting of ICG-HNPCC with the Leeds Castle Polyposis Group (LCPG), and paved the way for the ultimate amalgamation of the two groups in Cleveland, 2003. As LCPG met every two years, the next combined meeting was scheduled for 1999.
- 1998 Coimbra, Portugal. ICG-HNPCC meeting organized by Julio Leite
- 1999 Lorne/Melbourne, Australia: the second combined meeting of ICG-HNPCC and LCPG, organized by Finlay Macrae
- 2000 Tiberias, Israel. ICG-HNPCC meeting organized by Paul Rozen
- 2001 Venice, Italy: the third combined meeting of ICG-HNPCC and LCPG, organized by Lucio Bertario.

The HNPCC Council initially thought that it might be best to keep the group to a maximum of about 50 members. However, we soon realized that interest in HNPCC around the world was increasing almost exponentially, commensurate with numerous publications

appearing on the subject and the discovery of the existence and function of the DNA mismatch repair genes. Membership in the group has since been unrestricted and has reflected the broad range of specialties and disciplines involved in the scientific and clinical aspects of HNPCC. Collegiality among the membership became something to behold! Projects began emerging rather rapidly. They were discussed during the annual meetings and constructive ideas were constantly proposed.

### Contributions

Some of the key contributions to the study and management of HNPCC include publication of amended Amsterdam criteria allowing inclusion of extracolonic cancers in the clinical definition of HNPCC [2], publication of the Bethesda criteria to identify tumors likely to show microsatellite instability [3], the only collaborative study of the risk of rectal cancer after colectomy and ileorectal anastomosis in patients with colon cancer and HNPCC [4], and a multicenter study of mutation detection rate in patients with suspected HNPCC [5]. Currently, an important chemoprevention study is under way in Europe, with results expected in the near future (CAPP study II, Concerted Action for Polyp Prevention). In addition to these important studies, and others, the ICG-HNPCC maintains a database of known mutations in the mismatch repair genes. This has been of great usefulness in determining the significance of mutations as they are reported.



Figure 4. Attendees hard at work formulating the Amsterdam criteria: ICG-HNPCC meeting in Amsterdam, 1990. Photo courtesy of Hans Vasen.

### ICG-HNPCC and the Leeds Castle Polyposis Group

When the ICG-HNPCC was founded, few of its members had a particular interest in familial adenomatous polyposis (FAP). Neither *APC*, nor the mismatch repair genes had been discovered, and the Leeds Castle Polyposis Group membership was focused on issues related to FAP. In 1991, the gene responsible for FAP was cloned, and identification of the mismatch repair genes involved in HNPCC followed quickly. The overlap in interest for members of LCPG and ICG-HNPCC grew and it was natural that informal discussions start about uniting the two groups.

In 1999, at the combined meeting of ICG-HNPCC and LCPG in Lorne, Australia, these discussions became formal. In 2000, at the ICG-HNPCC in Tiberias, Israel, a new ICG-HNPCC Council was elected, including Lucio Bertario as Chairman of both ICG-HNPCC and LCPG, and James Church as Chairman Elect of both groups. In Venice, in 2001, the membership of the two groups approved a proposal to form a new international society for hereditary gastrointestinal tumors. Since then, the Joint Councils have been active in creating a constitution and an administrative structure for the new organization, to be known (courtesy of a suggestion by John Burn) as InSiGHT (International Society for Gastrointestinal Hereditary Tumors). As this new

society comes into being, it is important to remember and acknowledge the founders of ICG-HNPCC and the role that this group has had in expanding knowledge of HNPCC and improving care for patients and families affected by it.

### References

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