



THE HUMAN VARIOME PROJECT

Bulletin

From the Editor

This period saw a major turnaround in the funding fortunes of the Human Variome Project. First we learnt of promised financial support of the Victorian State Government for the Human Variome Project (HVP).

On 31st October, Prof. Richard Cotton, in his capacity as the Convenor for the Human Variome Project, hosted a dinner for the delegation from China in Washington. The

delegates include Prof. Ming Qi, who is an avid collaborator and supporter of the Human Variome Project in China.

Significant milestones were also notched during this period. We were pleased to report on the incorporation of the Human Variome Project, the establishment of the International confederation of countries advisory council and country nodes, the launch of

the Human Variome Project Malaysian Node in October and the success of the Function hosted by the Victorian Governor Professor David de Kretser on behalf of the Human Variome Project in August.

The Editor,
Alfreda Soetopo

Funding for the Human Variome Project

The Victorian State Government in Australia has announced on the *Victorian Biotechnology Action Plan: Biotechnology in Victoria – Meeting Challenges, Delivering Solutions* which highlighted a significant contribution of funds of A\$2.5 million over three years towards the global coordination of Human Variation Project. The support means that the Human Variome Project global Coordinating Office will be able to continue the work from Melbourne, Australia,

which is already one of the top five locations in the world for biotechnology. The Human Variome Project is committed to reducing the burden of genetic disease on the world's population by providing standards, systems and infrastructure for the sharing of information on all genetic variation (mutations) causing human disease. The free and open sharing of information on genetic variation and its consequences among scientists and

within society allows treatments to be delivered more effectively to patients and new treatments and cures to be developed. The funding will thus allow the office to continue its leadership role in supporting an international consortium of scientists, doctors and bioinformaticians working toward the capture and sharing of information on genetic variants of human disease.

Human Variome Project

Special points of interest:

- Funding for the Human Variome Project
- Launching of Malaysian Node of the Human Variome Project

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Government House Function in Support of the Human Variome Project

Professor David de Kretser AC, Governor of Victoria and Mrs. Jan de Kretser hosted a reception in support of the Human Variome Project (HVP) on 2nd August 2010 at the Melbourne Government House. Among those who attended this prestigious event were Sir Gustav Nossal AC, Ms. Jane Halton (Secretary, Dept. of Health and Aging), Mr. David Davis (State Parliamentarian) and the Hon. Alex Chernov (Chancellor of the University of Melbourne). In his speech, the Governor outlined the need for the collection of genetic variation information because it is the infrastructure on which critical research and treatment is based. The event was aimed to raise funds for the Australian collection activities and global coordination of the Human Variome Project. The speeches made at the Government House Function by Prof de Kretser, Sir Gustav Nossal, Prof. Richard Cotton and Mr. David Abraham (Chairman of the CASS Foundation) can be accessed at the following site:

<http://www.humanvariomeproject.org/index.php/news/speeches>

“The Human Variome Project will build the infrastructure on which critical research and treatment is based.”

**Prof. David de Kretser, AC,
Governor of Victoria**

Launching of Malaysian Node of the Human Variome Project

Report by Associate Prof. Dr. Zilfalil Bin Alwi [\[zilfalil@kb.usm.my\]](mailto:zilfalil@kb.usm.my)

The Malaysian node of Human Variome Project (HVP) is represented by the 1Malaysia Human Genome Variation Consortium (1MHGVC) which comprises of 52 researchers from 11 Malaysian universities and institutes. The project is headed by Associate Prof. Dr. Zilfalil Bin Alwi. The launching of the Malaysian node of the HVP was held on Oct 9th, 2010 at the Medical Faculty of Universiti Putra Malaysia, Serdang. The event was officiated by Dr. Vilasini A/P Pillai N.V. who represented Professor Emeritus Dato’ Zakri Abdul Hamid, the Science Advisor to the Prime Minister of Malaysia.

The event was attended by 125 participants comprising of scientists, researchers, medical doctors, paramedics, lawyers, postgraduate students, members of Parent Support groups and interested members of the public. The Genetics Society of Malaysia and the Medical Genetics Society of Malaysia co-sponsored the event. Professor Richard G Cotton from Melbourne, Australia, who is also the head of the Human Variome Project delivered a lecture on the HVP.

Later Professor Richard G Cotton along with Dr. Vilasini A/P Pillai and the representative from Ministry of Science, Technology and Innovation Malaysia (MOSTI) as well as the presidents of the Genetics Society and the Medical

Genetics Society of Malaysia signed on a plaque to mark the launching of the Malaysian node.

Besides the launching of the Malaysian node, the 1Malaysia Human Genome Variation consortium website and the national Malay whole genome SNPs database were also launched. There was also a multimedia show on the 1MHGVC and the HVP which was very entertaining and informative. More information on the 1MHGVC can be obtained from:

<http://1mhgvc.kk.usm.my/>

Through the HVP, the consortium hope to share the information contained in the unique datasets of Malaysians with the international community.



Left: Prof. Richard G Cotton, the Head of HVP, officially launched the Malaysian node of HVP.
Right: Prof. Richard Cotton giving a lecture on the Human Variome Project.



AP Dr Zilfalil Bin Alwi, Prof Dr. Mohamad Osman (President Genetics Society of Malaysia) and Prof. Richard G. Cotton listening to the speech of Dr. Vilasini A/P Pillai N.V along with other participants.



Assoc. Prof Dr. Zilfalil signing the plaque to mark the launching of the Malaysian node of HVP.



Members of the organizing committee



The members of consortium enjoying their dinner



A group picture of the consortium members along with the participants of the event, Dr. Vilasini A/PPillai N.V. (representing Professor Emeritus Dato' Zakri Abdul Hamid), AP Dr Zilfalil Bin Alwi (Head of 1MHGVC) and Prof. Richard G Cotton (Head of HVP).

Human Variome Project Incorporated

As of the 13th of October, in line with the Project Roadmap which was approved by the delegates of HVP3 meeting earlier this year, the Human Variome Project has now been incorporated to become Human Variome Project International Limited, an Australian Public Not for Profit Company limited by guarantee. Part of this process has been the establishment of an International Board of Directors and an International Scientific Advisory Committee. Members of the company are Sir John Burn (UK), Jean-Jacques Cassiman (Europe), David Rimoin (USA), Richard Cotton, David Abraham and Eric Haan (AUS). The Members appoint 3 Directors to the HVP Board. The Interim Board has been established with 3 Directors being appointed by the members; an election is presently underway to appoint the 3

HVP Scientific Advisory Committee elected May 2010, UNESCO, Paris

Arleen Auerbach	USA
Marc Greenblatt	USA
Garry Cutting	USA
David Rimoin	USA
Mireille Claustres	France
Mona El Ruby	Egypt
Finlay Macrae	Australia
Yoichi Matsubara	Japan
Gert-Jan B. van Ommen	The Netherlands
Johan T. den Dunnen (alternative)	The Netherlands
Mauno Vihinen	Finland
Christine Van Broeckhoven	Belgium
Aida Falcon Vargas	Venezuela

directors voted by the International Scientific Advisory Committee. In Paris at UNESCO Headquarters in May, the Interim International Scientific Advisory Committee was elected (see box above). They also elect 3 members of the Board.

International Confederation of Countries Advisory Council and HVP Country Nodes Established

The next step is the formation of the International Confederation of Countries Advisory Council, a representative body made up of delegates from each HVP Country Node. The International Confederation of Countries Advisory Council (ICCAC) is composed of one representative from each of the HVP Country Nodes – secure online repositories of all genetic variants being discovered in the diagnostic laboratories of individual countries which will not only be valuable sources of information to inform better diagnostic decisions and healthcare planning within the countries possessing nodes, but will also share portions of their datasets with international gene and disease specific databases. The nodes are responsible for collection of all instances of all mutations in all genes in

their country which could easily be adapted to serve as a disease registry.

Representatives of ICCAC are appointed by their respective Nodes; the Chair is elected by the membership of the Human Variome Project Consortium present at the HVP biennial meetings. Individual countries can apply for membership of the International Confederation of Countries. When accepted they will formally become a Country Specific Node of the Human Variome Project with a representative appointed to the ICC advisory committee. The purpose of these nodes is to support and promote the standardized collection of genetic variation information within the country, and to assist in the formation of international policy

concerning Genetic Variation. Currently six countries have signed up: Australia, Belgium, China, Egypt, Kuwait and Malaysia.

A detailed policy document outlining how a country can become a full member of the International Confederation of Countries Advisory Council can be found at:

<http://www.humanvariomeproject.org/index.php/publications/policy-documents/131-partner-country-node-policy>

Those interested in starting a consortium within their own country and joining the International Consortium of Countries should contact Richard Cotton [cotton@unimelb.edu.au]

Human Variome Project International Limited is now an affiliate member of IFHGS

The application for the Human Variome Project International Limited (HVPI) to join the International Federation of Human Genetics Societies (IFHGS) as an affiliate member was accepted on 15 November. As a corresponding member, HVPI will be notified of all meetings of the Federation Executive Committee and will be invited to suggest items for the agenda.

Report on Working Meeting of Spastic Paraparesis Mutation Database 12-14 September 2010, Burgos, Spain

Provided by **María-Jesús Sobrido**
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Within the scope of the Human Variome Project, neurogenetics initiatives are being started to coordinate international, multidisciplinary, disease-centered mutation databases for neurological disorders. In order to start such a database specifically for hereditary spastic paraparesis (HSP), a working meeting was held on September 12-14, 2010 at the Spanish National Reference Center for Rare Diseases and their Families (CREER), Burgos. The HSPs are a group of neurodegenerative conditions affecting the motor neurons with large clinical and genetic heterogeneity, and thus exemplify what is the general case for most genetic disorders of the nervous system. Experts in the clinical, genetic, and cellular aspects from the US and several European countries, as well as bioinformaticians met to discuss the problems and delineate actions towards the

construction of a coordinated collection and curation of all genetic variations identified in HSP genes and their associated clinical manifestations.

Issues such as database fields, coding and collection, reference sequences, informatics structure, pathogenicity assessment, funding and ethical and legal aspects were discussed and a vision and plans document was produced at the end of the meeting. The attendees at the HSP starting workshop decided to build an LOVD-based database customized to the needs of motor neuron disorders, focused in the genetic variation but adding relevant clinical information. Further agreements were to pursue a multidisciplinary evaluation of pathogenicity, to establish consensus reference sequences, to include family and control population information and to establish an ethics oversight committee, among others. An XWiki-based manage-

ment was adopted as communication platform for the working group. The need for seed funding to be able to produce a pilot, curated HSP mutation collection within a year's frame was a main question. The HSP database consortium will seek integration with other relevant groups working in related areas, as well as support and encourage the exploitation of the data by the scientific and clinical communities.

This HSP database effort will be pursued within the frame of the wider Neurogenetics consortium, which in turn emanates from the Human Variome Project initiative and vision. Clinicians and scientists worldwide interested in spastic paraparesis and motor neuron disorders are welcome to join this ongoing initiative.

Report on NIH Colon Family Cancer Steering Committee Meeting Dallas, Texas, Oct 10th and 11th

Report by **Prof. Finlay Macrae**
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The CFR is a consortium of centres funded by the US National Cancer Institute, responsible for establishing and maintaining a valuable resource of probands with colorectal cancer, and their extended families. Recruitment in some centres is through population based approaches, in others through familial cancer clinics, and in some, both. The Australasian node of the CFR has had both forms of recruitment. Other nodes of the CFR are at UCLA (which includes the Cleveland Clinic and Dartmouth Medical College, Hew Hampshire), Mayo Clinic, University of Hawaii, Fred Hutchinson Cancer Centre, Seattle and Toronto. The core investigators are skilled at US grantmanship, and strong in genetic epidemiology, but also encompass a wide range of relevant skills with a stakehold in mismatch repair research.

The Steering Committee meets face to face twice a year, and by teleconference, monthly. The purpose of the CFR is to assemble detailed personal and family histories of the probands, and their relatives, with cascade recruitment across families, commencing with the proband. In addition, there is banking of tumours, both as paraffin blocks and, where possible, frozen sections, and lymphocytic DNA. Cell lines have been developed from the latter. MS and immunohistochemistry for the MMR proteins have been performed on tumours biobanked, and DNA has been analysed for tumour directed analysis of relevant MMR gene.

The CFR is not a hypothesis driven establishment. Rather, it depends on investigators within its ranks, and outside its ranks, to drive research questions and analyses based on the resource available. There is an active process of encouraging outside investigators to utilize the resource.

Much of the meeting was administrative, relating to the processes of data cleaning, biobanking, translation of research findings, and appreciation of the applications to the CFR for scientific enquiry. However, for the October meeting, there was a particular emphasis on sustaining the core CFR infrastructure beyond August 2012, as the NCI has not approved the renewal grant recently submitted. Alternative NIH funding mechanisms were the focus of the meeting, including a U01 grant process which supports core infrastructure for cohorts, but in a much more competitive field across the broad range of cancers.

Continued on page 6 ...

Report on NIH Colon Family Cancer Steering Committee Meeting Dallas, Texas, Oct 10th and 11th

...Continued from page 5

Building on the establishment of a worldwide consortium of interests in mismatch repair which was spawned at the Dusseldorf InSiGHT meeting of the CFR SC, and further at its Washington meeting in April, a new consortium now known as the International Mismatch Repair Consortium (IMRC) was bedded down. The consortium with nearly 30 members, is largely derived from the CFR and InSiGHT members, approached by the InSiGHT executive to join the consortium. The consortium has access to over 10,000 carriers from 3800 families, increasing the power of studies available by over 20 fold. There is no universal data collection for epidemiological studies across the consortium, but nevertheless what is collected is a rich source of data to be mined. The development of this consortium has been a key interest of InSiGHT this last year. The marriage with the CFR will bring complementary skills to the table – principally genetic epidemiology from the CFR and clinical and functional assay experience relating to unclassified variants from InSiGHT.

The IMRC will move forward with 2 R01 grants next year. The first, with PIs Robert Haile (UCLA), Mark Jenkins

(MEGA, Melbourne) and Finlay Macrae (RMH and InSiGHT) will have penetrance as its theme (penetrance by gene, by ethnic group, by country, by gender, and possibly by mutation including missense variants). It will cover modifier gene studies, and lay the groundwork for further studies of pathogenicity of unclassified variants. The second R01 grant will focus on functional assay development and deployment to clinical laboratories, coupled with computational biological approaches to interpretation of these missense variants, ultimately quantitated (for pathogenicity) through a Bayesian Likelihood Analysis. InSiGHT will lead this endeavor, with PIs from Europe and USA.

The IMRC is bound to expand further, through encouragement of and by InSiGHT, to include the middle east, Africa, and South America, as well as the Scandanavian countries.

Further efforts to collect clinical outcome data, including surveillance findings, was also considered to be essential to reap the benefits of this CFR valuable resource. Within the CFR, a study on metachronous cancer stratified by extent of surgery was pre-

sented by Susan Parry from New Zealand – a project conceived at the Dusseldorf InSiGHT combined meeting with the CFR.

The CFR has been slow to implement a chemoprevention trial, but is now working actively to support InSiGHT's CAPP trials; a proposal to add an arm including DFMO to a dose finding aspirin chemoprevention trial was supported at the meeting. This will go forward to the CAPP committee, chaired by Sir John Burn in Newcastle. Australia, through the CAPP trial centre at The Royal Melbourne Hospital, contributed strongly to the CAPP2 trial, and looks forward to the CAPP3 trial. We learnt also of the opening of the ANVIL trial in Germany, the first RCT of a vaccine against the neo-peptides characterizing MSI in tumours.

It was not all organizational. There was interesting reports of Work in Progress on exomics (exonic sequencing) of non-Lynch, non FAP familial colorectal cancer, mostly type X. The likely gene loci were being closed in on through this approach at the Mayo Clinic, using the CFR resources. The QIMR is taking a similar approach to hyperplastic polyposis without a signal achieved yet.

Announcements

Best Wishes to Sue Povey

Unfortunately Sue Povey has had to resign from her position as Chair of the Ethics Committee Working Group. We would like to acknowledge and thank her for her efforts and great contributions over many years.

Congratulations Aida!

We would like to congratulate Aida Al Aqeel for receiving the Prince Sultan Prize for Pioneers in Innovations and Health Sciences. We look forward for further collaborations with her.

“The curator will be responsible for, amongst other things, the integrity of the database, promoting further submissions, and controlling access to the database to bona fide users.”

InSiGHT mismatch repair curator appointed in Melbourne!

InSiGHT, the peak international body for health professionals with an interest in familial GI cancer, has maintained a database of mismatch repair variants identified in familial bowel cancer families, over the last 15 years. This database is a very valuable resource to assist in classifying any findings from mutational analysis of these genes as is done regularly around the world, and in Victoria, by Genetic Health Services Victoria (Desiree Dusart's team), Peter Mac (Alex Dobrovic), and GT technologies.

Maintaining the integrity of this database has been done pro bono until now, by Paivi Peltomaki in Helsinki, and Mike Woods in St Johns Newfoundland. With the number of variants submitted increasing from 550 to 13000 over the last 2 years,

the task is now beyond pro bono assistance.

Enter the Hicks Foundation! The Hicks Foundation has recognized the extreme importance of this database for the sake of all stakeholders including families with interests in MMR variants, and its alignment with the Human Variome Project. The Hicks Foundation Curator of the InSiGHT database has recently appointed. The curator will work from the Human Variome Project offices at the Howard Florey, University of Melbourne, and be supervised by a number of InSiGHT experts in the field, as well as Professor Cotton at the HVP.

InSiGHT, and the HVP welcomes John Paul Plazzer to this new and exciting role. He will be responsible for the integrity of the database,

promoting further submissions, searching the literature for information on MMR supported by the automated searching programs being developed by Lawrence Cavedon and Tim Smith for the HVP, annotating the database with information relating to function and structure of MMR variants, assisting in organizing our team of experts assign pathogenicity to variants of uncertain significance (a really important task) and controlling access to the database to bona fide users.

Finlay Macrae

Secretary, InSiGHT

Deputy Director, Genomic Disorders Research Centre.

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Publications of Interest

"Human Variome Project on Target to Collect All Genetic Data" - 2 November 2010 <http://www.humanvariomeproject.org/index.php/news/press-releases>

Kaput, J, Evelo, CT, Perozzi, G, van Ommen, B and Cotton, R. Connecting the Human Variome Project to Nutrigenomics. *Genes and Nutrition* (2010) 5: 275-283.

Kohonen-Corish, et al. How to catch all those mutations – The Report of the third Human Variome Project Meeting; UNESCO Paris, May 2010. *Human Mutation* (2010), 31 (0) DOI: 10.1002/humu.21379

Povey, et al. Practical Guidelines Addressing Ethical Issues Pertaining to the Curation of Human locus-Specific

Variation Databases (LSDBs). *Human Mutation*, 31(11):1179-84, 2010.

Laurila, JB, Naderi, N, Witte, R, Riazanov, A, Kouznetsov, A and Baker, CJ. Algorithms and semantic infrastructure for mutation impact extraction and grounding. *BMC Genomics* 2010, **11**(Suppl 4):S24

Ashley, EA, Butte, AJ, Wheeler, MT, et al. Clinical assessment incorporating a personal genome. *Lancet* (2010), 375: 1525–35.

Stenson, PD and Cooper, DN. Editorial. Prospects for the automated extraction of mutation data from the scientific literature. *Human Genomics* (2010) 5(1):1-4.

Bateman, A. Editorial. Curators of the world unite: the International Society of Biocuration. *Bioinformatics* (2010) 26(8): 991.

Smedley, D, Schofield, P, Chen, CK, et al. Finding and sharing: new approaches to registries of databases and services for the biomedical sciences. *Database* (2010) DOI: 10.1093/database/baq014.

Patrinos, GP, et al. Recommendations for genetic variation data capture in developing countries to ensure a comprehensive worldwide data collection. *Human Mutation* (in press – to be published in January 2011 as Special Article)

Cotton, RGH, Vihinen, M and den Dunnen, J. Genetic Tests Need the Human Variome Project. Letter to the Editor. *Genetic Testing and Molecular Biomarkers* (in press - to be published in Jan/Feb 2011)

Perspective

Variomic Health Care in Japan – a personal commentary

Joji Utsuomiya MD

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To involve in HVP for the ones who theoretically regard it necessary, a proper financial background is essential, because it is an infrastructure not providing immediate merit to investigator. For raising a fund, at least until now, HVP itself has not been hardly appreciated as an aim of the research project as well as a target for donation as a cooperate social responsibility(CSR). To implement HVP, in this regard, collaboration with the research project involving the personalized medicine is reasonable because they need the variation database. This could be a bottom-up approach that would begin by the needs and wishes of entrepreneur, rather than a market opportunity or a 'top-down' approach.

Chemoprevention on hereditary cancer and food company

A productive approach like interventional prevention will be appreciated by researchers, clinicians as well as patients and variations will be collected efficiently by this way.

To organize LSDB for familial polyposis I am attempting to activate a project about clinical application of the result issued by University of Colorado Denver, Aurora, CO, USA; which identified dietary feeding of "grape seed extract (GSE) inhibited intestinal tumor in

mouse model with apc mutated¹.

As a core clinical investigator, Hideki Ishikawa MD² who has a sustainable research group for cancer prevention in FAP for many years has agreed with my suggestion for clinical trial of the Colorado study. To raise funds, I am asking for help from Mr. Akira Matsumoto CEO of the Calbee Foods Co LTD. He is now examining on the issue with one of his collaborators, Pepsi Co. Involvement of those two food companies must be appreciable in regards to popularization of HVP. We hope anybody in HVP group in the world could encourage them for positive action on the project.

Personalized prevention of the "lifestyle relating disease" as a business model in Osaka

In 2000, the concept for "the life style relating disease" as a national project has started to reduce ever increasing medical service cost. "Signpost" (<http://www.signpost.corp.com/index.html>) is the Osaka University bioventure company which has yielded a new business model of personalized prevention of the life style disease³. The president Yoshiyuki Yamazaki MD has founded this model based on his clinical longitudinal observatory study on diabetic patients who have the natural course of vascular sclerosis and modification of the trend that was found predicted by combination of a series of SNPs⁴. The research group that he has developed has created a database involving 6000 patients to predict individual risk for vascular complication and serve for preventing those by nutritional as well as physical exercise course. With a help of the Douglas Laboratory. Dr Yamazaki is now inviting those institutes or clinics that are willing to collaborate with him.

Ongoing reform in health care policy at the Metropolis Tokyo

At the Komagome Hospital that has become the metropolitan center for cancer and infectious disease, I had a session on HVP last November and met with Dr Hisahi Sakamaki, hematologist and vice President of the center working as a chief of the taskforce for remodeling operation who is planning a center for tissue bank and genetic counseling. I have suggested him to include a function of the personalized prevention with HVP there. We have agreed to be co authorship for a Japanese review article on HVP⁵.

Inflammatory Bowel Disease (IBD) Center in Hyogo

Functional proctocolectomy with ileoanal pouch is now globally recognized as a standard technique for cancer preventive surgery for FAC and UC. It has been invented by myself in Tokyo Medical and Dental University in 1978 and introduced to Hyogo College of Medicine in 1983. In 2009, the IBD center has been founded in Hyogo⁶ where 1,200 patients of UC and 730 of Crohn disease have been registered. About variants for CD, GWAS have recently identified more than thirty CD-associated genes/regions in the European population. In the East Asian, however, clear associations between CD and those genes has not been identified yet⁷, and have suggested a presence of Asian specific variomic profile. Hiroki Ikeuchi, an associate chief of the center and one of my pupils is maintaining clinical data for 30 years so carefully that we can produce an independent LSDB which would be useful for personalized management of IBD.

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Variomic Health Care in Japan – a personal commentary

How I have been involved in HVP?

A direct opportunity was the InSiGHT meeting at Yokohama 2006 where I, as the honorable president, made the opening lecture entitled as “Polyposis study and my life”⁸ and concluded that promoting HVP should be one of the result of the meeting. As a result, Drs. Richard Cotton, Finlay Macrae and myself have agreed to start the Insight and HVP collaborative project as a pilot.

Originally I started my professional carrier as a surgeon in Tokyo Medical and Dental University 1954 and took post-doctorate training under Dr George Woolley, a geneticist in Memorial Sloan-Kettering Cancer Center from 1960. My thesis was testing oncogenic activity of the nucleic acids extracted from cancer tissue. As a result, my work have been focused on polyposis and hereditary cancer to have developed the Polyposis Center in 1974 ,the third in the world that had collected the largest number of confirmed pedigrees to elucidate oncogenesis in hereditary tumors through collaboration with the authorities including Drs Victor Mc Kusick, Alfred Knudson, Henry Lynch etc. The centers served not only for creating the new surgery but also for detecting the gene. In 1991, apc has been identified, as the first responsible gene for common cancer, by Dr.Yusuke Nakamura and our group. This then has disclosed the phenotypic heterogeneity like polyp density subtype are determined by mutation site on the gene and the predictive diagnosis for FAP has been succeeded by 1995 when US NCI Cancer Genetic Project chaired by A Knudson has started.

Occasionally paralleled with him, I have been involved for 10 years in the project for constructing Cancer Genetics Infrastructure by the Department of Health Welfare that included initiating the specific research society, editing ELSI guide line, holding a seminar for genetic counselor, starting a cancer genetic clinic in JFCR hospital, promoting commercial germ line genetic test, and constructing phenotype/genotype database The last one is the most important but more difficult above all because the pedigree database for hereditary cancer that include enormous amount of data on case and family accumulated during several decades of year have been frozen or unknown because of a spread of very strict Japanese bioethical revolution around the New Millennium period .Since then medical investigators have become sometimes too much reluctant or fear about treating with risky personal and family information.

In those situations, I have realized HVP may open another entrance of approach to the goal of personalized medicine by collecting variation instead of collecting pedigree.

Appendix

1. Balaiya Velmurugan, Rana P. Singh, Nidhi Kaul*,Rajesh Agarwal and Chapla Agarwal ,Dietary Feeding of Grape Seed Extract Prevents Intestinal Tumorigenesis in AP-Cmin/+ Mice1 Neoplasia 12: 95–102, 2010.
2. Ishikawa,H et al. Randomized trial of dietary fiber and Lactobacillus casei administration for prevention of colorectal tumors Int. J. Cancer 116: 762–767, 2005.

3. Personal style relating disease : It imply diseases such as diabetes , arteriosclerosis, and brain or heart bleeding or infarction
4. Yamasaki Y, et al. Combination of Multiple Genetic Risk Factors Is Synergistically Associated With Carotid Atherosclerosis in Japanese Subjects With Type 2 Diabetes. Diabetes Care 29: 2445-2451, 2006.
5. Utsunomiya J and H. Sakamaki, HVP and Hereditary CRC, GI Research to be published 2010
6. Ikeuchi H ,Utsunomiya,J et. al. Surgery for ulcerative colitis in 1000 patients (Submitted for publication); HVP should be sustainable as a Global Public Good, if at fundamental medical education, students learn genotype always attached with symptom as is in histology at present, the situation will be simple, but it is not so at moment here.
7. Nakagome S, Takeyama Y, Mano S, Sakisaka S, Matsui T, Kawamura S, Population-specific susceptibility to Crohn's disease and ulcerative colitis; dominant and recessive relative risks in the Japanese population. Ann Hum Genet. 74(2):126-36, 2010.
8. Utsunomiya J, T Iwama, M Miyaki K Tamura. M Arai,A historical perceptive for familial cancer; result and vision of Polyposis Center Project. Int Clin Onc. 9: 215-231, 2004.



THE HUMAN VARIOME PROJECT

Vision

The Human Variome Project will establish systems to collect and make available information on all genetic variations associated with human disease.

Mission

The Human Variome Project is dedicated to improving health outcomes by facilitating the unification of data on human genetic variation and its impact on human health. It supports the use of human variation information in clinical & research environments across the world.

Values

- Free public access to information
- Inclusive of all countries, peoples and disciplines
- Provision of appropriate credit and acknowledgement
- Respect ethical, legal and social issues



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Meetings of interest

Practical Locus Specific Database course: the Leiden Open source Variant Database example, a one day training workshop on 13 December 2010 offered by UCL Genetics Institute at University College London, UK. For further details, contact Sarah Leigh sarah.leigh@ucl.ac.uk

36th Annual Conference of Indian Society of Human Genetics and International conference on Genomics, Genetic Diseases and Diagnostics, 14-16 February 2011, Manipal life Sciences Centre, Manipal, India.
<http://ishg2011.manipal.edu/>

Pathology Update 2011, 4-6 March 2011, Melbourne Convention Centre, South Wharf, Melbourne.
<http://www.rcpa.edu.au/pathologyupdate/>

AMIA 2011 Summit on Translational Bioinformatics, 7-9 March 2011, San Francisco

<http://jointsummits2011.amia.org/>

The fourth biennial InSiGHT meeting, 30 March-2 April 2011, San Antonio, Texas.

<http://www.insight-group.org/meetings/texas2011/>

International Forum on Quality and Safety in Healthcare. 5-8 April 2011, Amsterdam.

<http://internationalforum.bmj.com/2011-forum/>

II Latin American Congress of Human Genetics (II CLAGH) and the VI National Congress of Biology. 11-13 May 2011, San Jose, Costa Rica.

<http://www.congresobiologiagenetica2011.info/>

International Mutation Detection Meeting, 6-10 June 2011, Santorini, Greece.

<http://www.mutationdetection.org/santorini/>