กฟผ.
ผลิตไฟฟ้าเพื่อความสุขของคนไทย

โครงการย่อย

การศึกษาความสัมพันธ์ระหว่างปัจจัยทางพันธุกรรมและปฏิสัมพันธ์ระหว่างปัจจัยทางพันธุกรรมกับสิ่งแวดล้อมกับการเกิดโรคมะเร็งที่พบบ่อยในชาวไทย(EGAT)

Genetic contribution and gene-environment interaction in cancer causation in Thai (EGAT)population

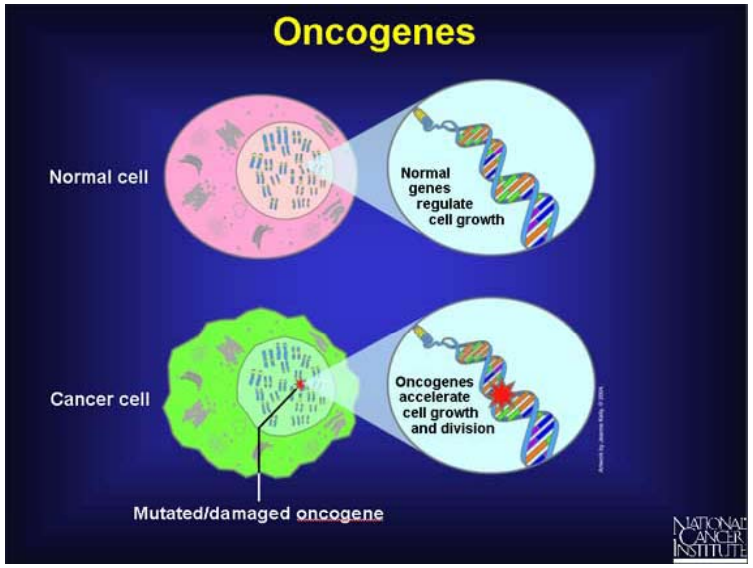
Thanyachai Sura, Jakris Eua-Soonthornwattana, Atchara Tunteerathum, Natini Jinawath, Donnipat Dejsuphong , Piyamitr Sritara

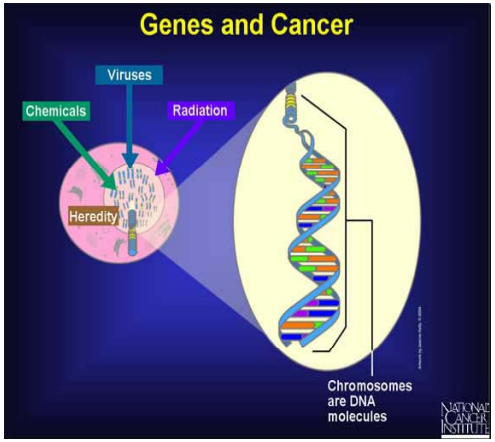
- **Cancer develops because of a complex mix of environmental and genetic factors.**
- **For some**:-
  - Environmental factors pose the greatest risk
- **For others**:-
  - It is inherited susceptibility
- **For most**:-
  - Combination of all the above.

Population of EGAT study

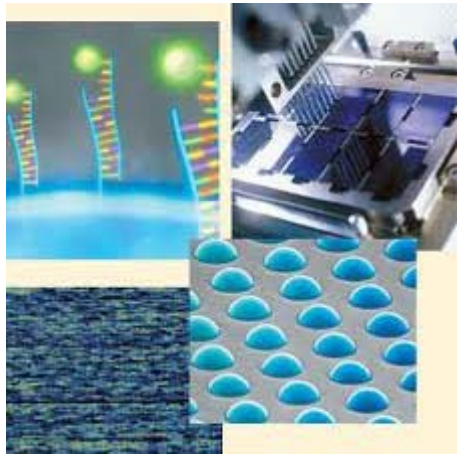
- EGAT 1 ~ 2,800
- EGAT 2 ~ 2,200
- EGAT 3 ~ 2,000

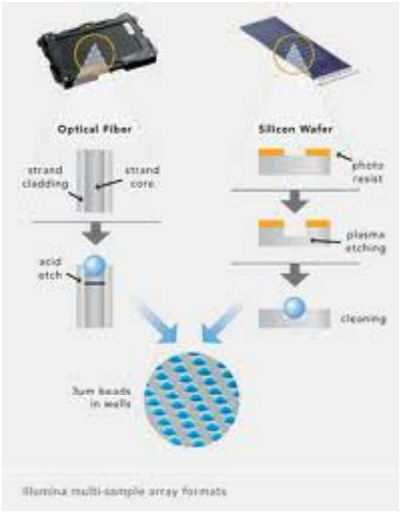
Cancers ~ 480

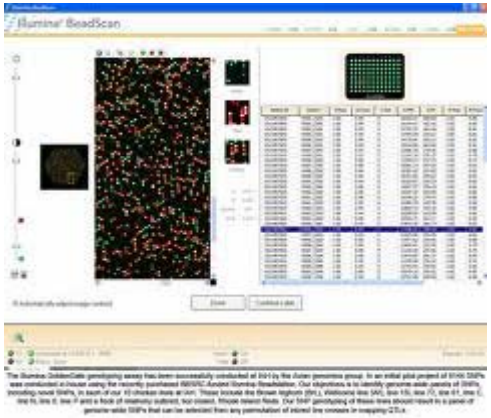


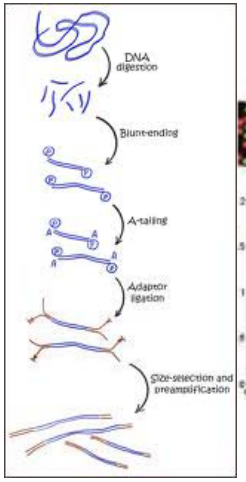


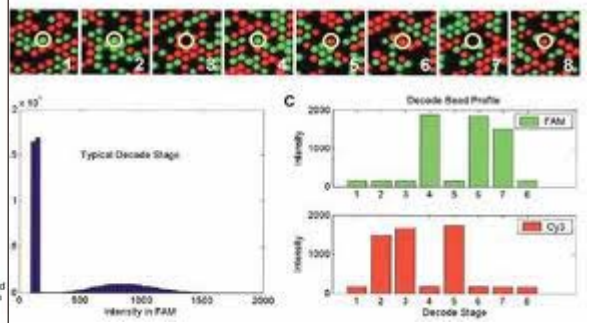
The number of **1440** samples have successfully been genotyped
on cancer SNP panels containing
~1,500 known cancer-related SNPs. .
The genotyping technology utilized is that of
Ilumina GoldenGate Genotyping Assay. .
Among the processed samples,
half are those that do not have cancers (“control”),
and half are those that have cancers (“case”).
Due to the diversity of cancer types,
clusters are made under the type of cacers .
Colorectal cancer has the greatest number
of cases and the significance SNPs are identified.
The next step is to verify the significant SNPs
to the other population for the most beneficial
genotyping in colorectal cancer in Thai population.




Optical Fiber
Silicon Wafer
strand cladding
strand core
photo resist
plasma etching
acid etch
cleaning
3um beads in wells
Illumina multi-sample array formats


Illumina BeadScan


DNA digestion
Blunt-ending
A-tailing
Adapter ligation
Size-selection and preamplification


Typical Decode Stage
Intensity in FAM
C
Decode Bead Profile
FAM
Cy3
Intensity
Decode Stage

The most strongly associated SNPs

(P = 1.72 10^{-7}, allelic test)

rs6983267

rs10505377

rs7841264

rs10505477 and rs6983267

rs6983267 and rs10505477

rs10505377 chromosome 2 , 3p
rs6983267 Mismatch repaired gene

Novel Non-hot spot *APC* mutations in Familial Adenomatous Polyposis (FAP) in Thai Families

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Background

FAP (OMIM#175100) is a predisposing colon cancer syndrome in which hundreds to thousands of precancerous colonic polyps develop usually at age 16 years. 95% of individuals have polyps at age 35 and high risk becoming malignant without colectomy.

Objectives

1. To study the incidence and correlate the genotype-phenotype relationship of germline mutation in *APC* genes in Thai Patients.
2. To encourage genetic testing for *APC* in at-risk pre-symptomatic patient.

Methods

All multiple colonic polyps with tissue pathology confirmed patients were reviewed their clinical courses and assessed other extracolonic features. Then, they were screened by direct whole gene sequencing for germline mutations in *APC*.

Results

We found 3 novel mutations at c.385G>C, c.559delA and c.3027delG at exon 3, 5 and 15, respectively in 3 unrelated families. Two children of the first family developed osteoma at age 5 and 7 year-old, respectively while the others have only family history of colorectal cancer without other extracolonic features.

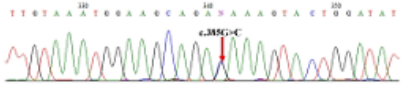

Fig 1. c.385G>C in family I-1 identified by sequencing.

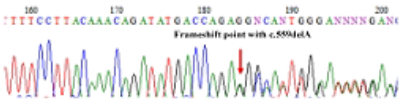

Fig 2. c.559delA in family II-1 identified by sequencing.

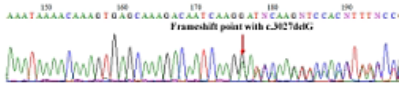

Fig 3. c.3027delG in family III identified by sequencing.

Table 1. Summary of *APC* mutations in Thai patients.

Family	*Relation*	*Age*	*Nucleotide Change*	*Protein Change*	*Clinical*
I-1	Index	33	c.385G>C	E129Q	Colonic polyps with osteoma
I-2	Offspring	7	c.385G>C	E129Q	-
I-3	Offspring	3	c.385G>C	E129Q	-
I-4	Offspring	2	No	No	-
II-1	Index	31	c.559delA	R187Gfs*18	CA rectum
II-2	Offspring	9	No	No	-
II-3	Sibs	34	No	No	-
III	Index	31	c.3027delG	N1070Ifs*56	CA rectum with liver metastasis

Conclusion

Disease-causing mutations in *APC* are high penetrance and predisposing to CRC. Our preliminary results discovered 3 novel mutations in which 2 of them are not located in frequently reported in exon 15. These results imply that targeted-mutation analysis may not sufficient to test in some populations. Ethnic variation may cause difficulty in genetic screening especially in large genes. However, we strongly recommend genetic test in at-risk group for early diagnosis and total colectomy before develop advanced CRC.

Acknowledgement

This work is the preliminary report dedicated to all patients and families who were affected from [illegible] in Thailand. We are thankful to our patients at Ramathibodi hospital for participation in this study. The study was supported by Medical Genetics Research Fund, Ramathibodi Foundation, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.

Correspondence

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e-mail: powerchanon@hotmail.com, e-mail: dolljoy1@hotmail.com ; e-mail: [illegible]

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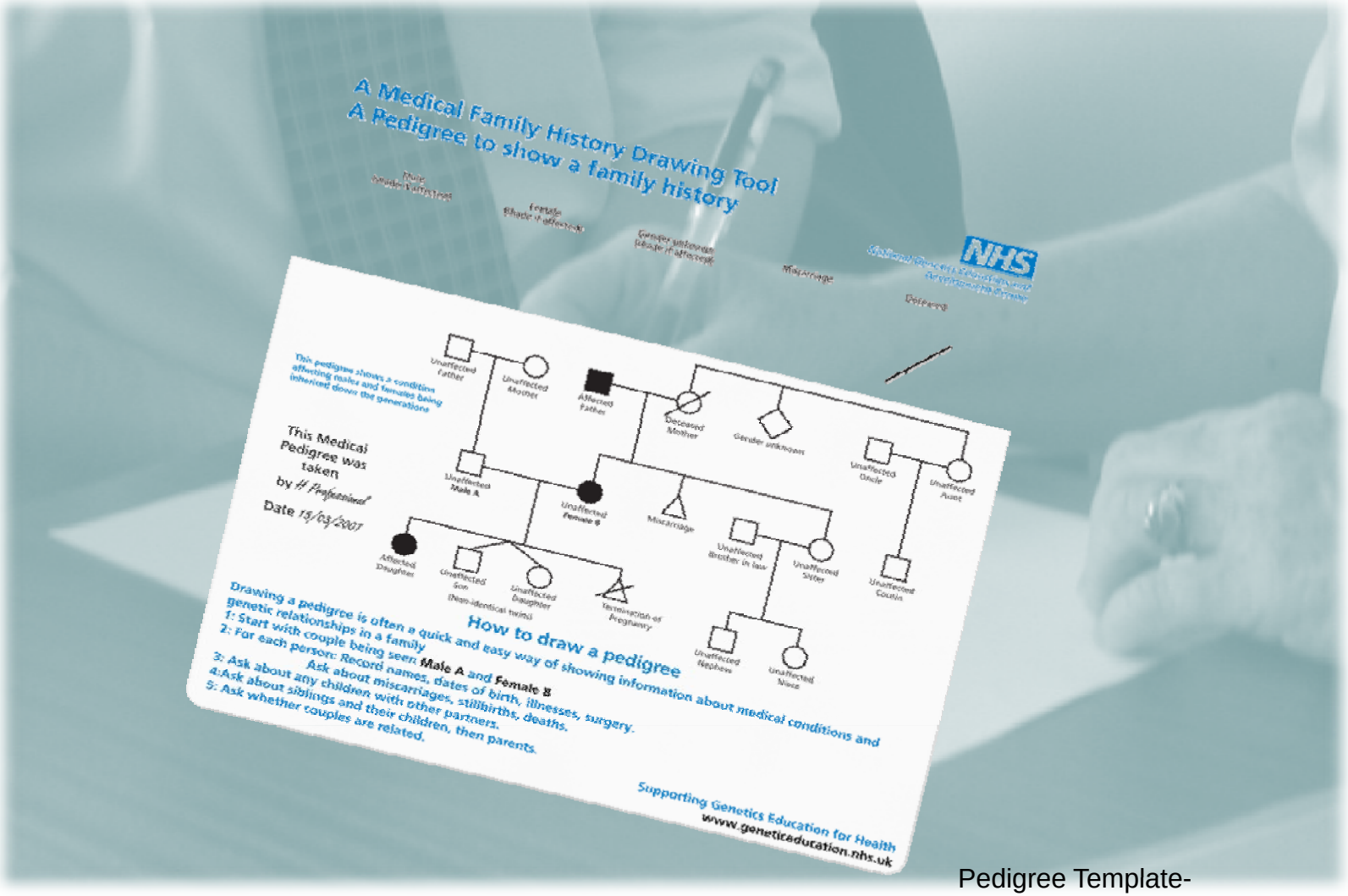
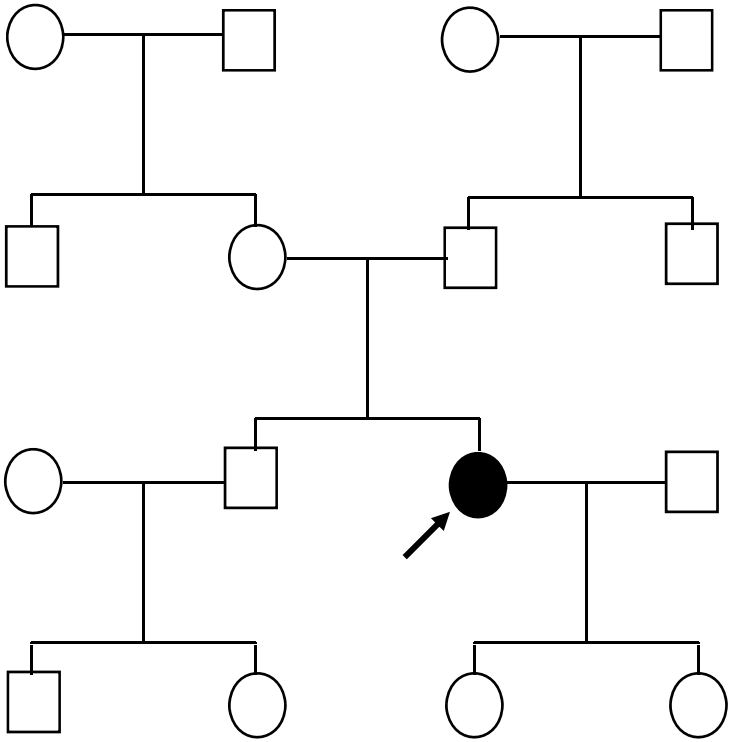
Drawing a pedigree



Pedigree Template-
One of the resources available from the NHS National Genetics Education and Development Centre

Half of the population have had a 1st or 2nd degree relative diagnosed with cancer



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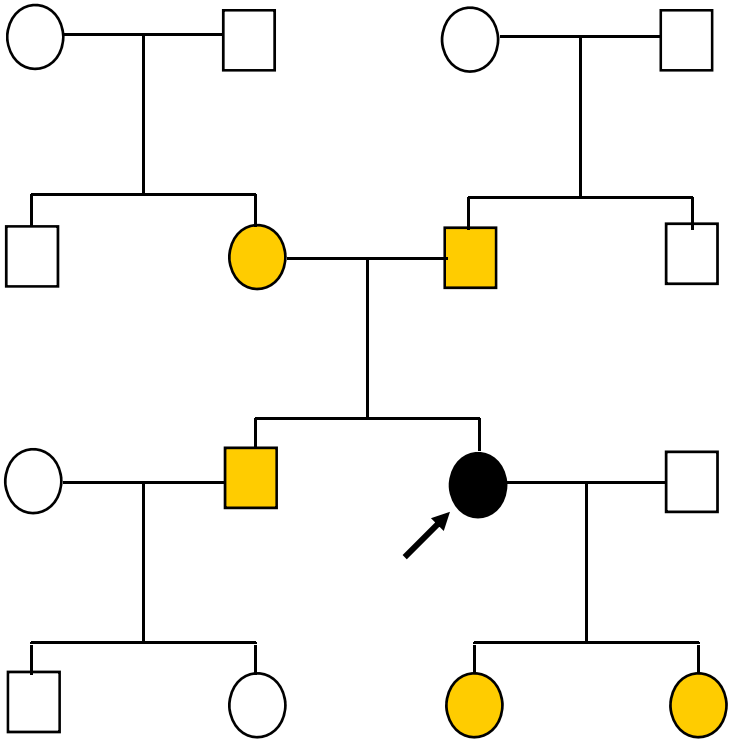
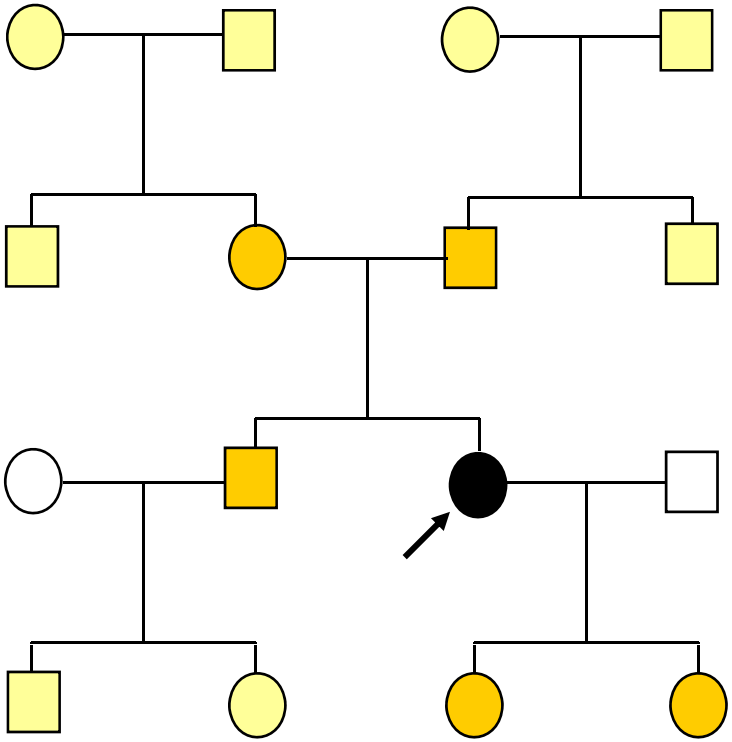


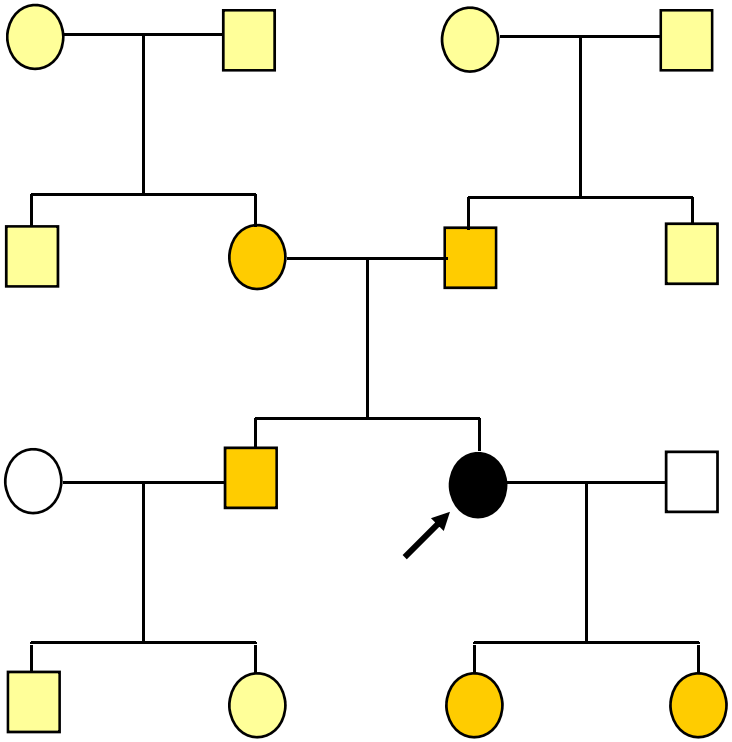
1st degree (parents, siblings, children)

Half of the population have had a 1st or 2nd degree relative diagnosed with cancer



2nd degree (grandparents, aunts, uncles, nieces, nephews)

Half of the population have had a 1st or 2nd degree relative diagnosed with cancer

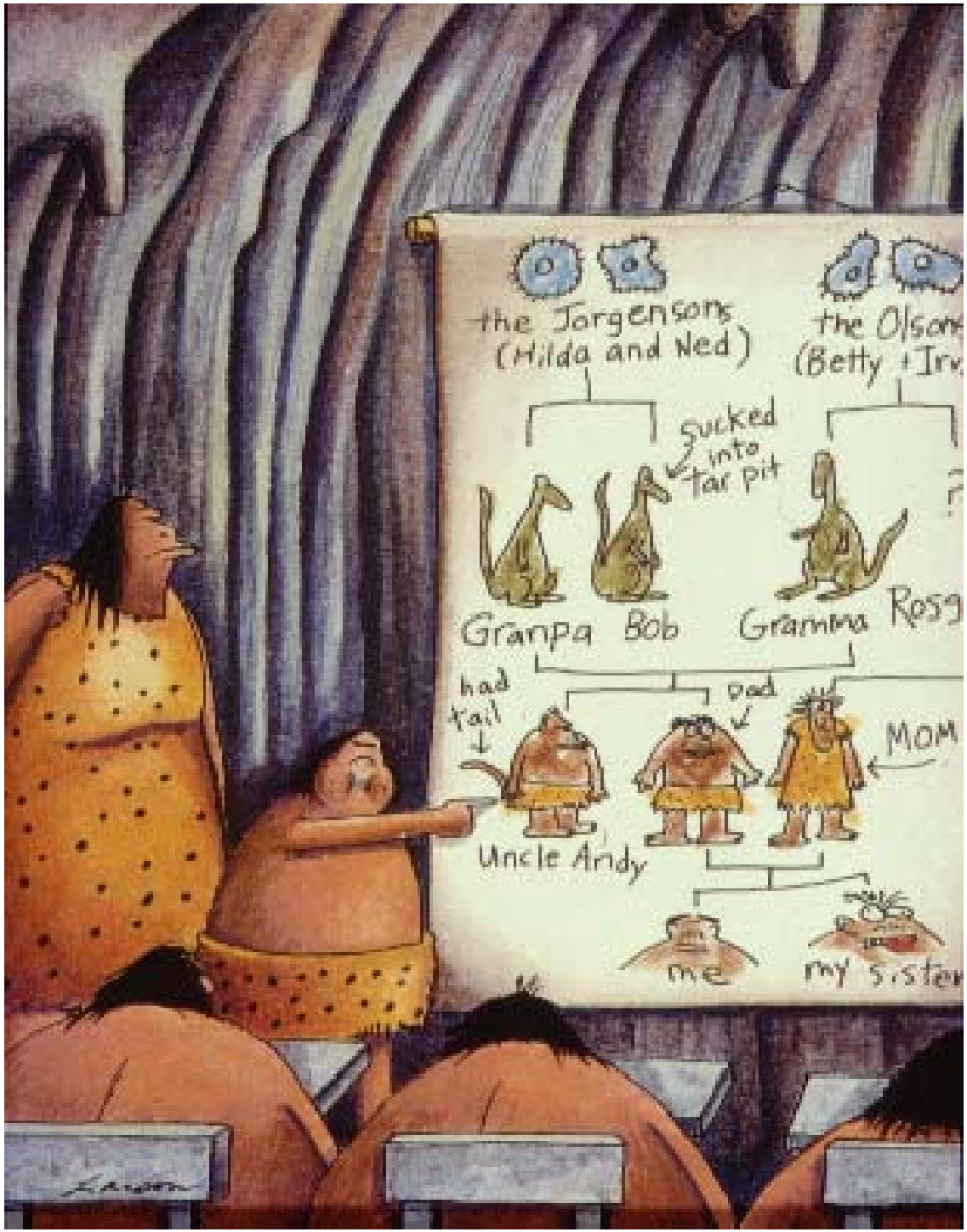


2nd degree (grandparents, aunts, uncles, nieces, nephews)

Only 5% - 10% will have an inherited genetic factor

The next step is :to verify the significant SNPs to the other population

Japan , Australia , Malaysia



Drawing up the family tree gives information about the relatives and also:

- **helps establish the family agenda and dynamics**
- **may reveal individuals interpretation and beliefs about what is happening in the family**
- **Has the potential to raise issues of paternity**

In summary…