

## Hereditary non polyposis colorectal carcinoma (HNPCC Syndrome)

### Identity

Other names Lynch Syndrome

**Inheritance** autosomal dominant ; frequency is about 1 to 2/1000 inhabitants; founder effect has been found in finnish population

### Clinics

**Phenotype and clinics** Hereditary non polyposis colorectal carcinoma is an autosomal dominantly inherited predisposition to develop [colorectal cancer](#), [endometrial carcinoma](#) and [ovary carcinoma](#), urinary tract carcinomas, stomach, small bowel and biliary tract carcinoma, and brain tumors. Colorectal carcinoma is characterized by early age at onset, predominantly right sided with an excess of synchronous and metachronous tumors.

**Neoplastic risk** The risk of colorectal cancer in HNPCC patients is estimates up to 75% by age 75. The average age of diagnosis is 45 years for colorectal cancer. It is interesting to note that the risk of colorectal cancer for women was less that observed for men and average age of diagnosis was delayed. The risk of uterine cancer in HNPCC female is estimated up to 40% and the risk of ovarian cancer is less than 10%. The risk of metachronous colorectal cancer, when limited resection of colon was performed, is estimated to 30%

**Treatment** Full coloscopy to the caecum is recommended every two years beginning at age 25 years or 5 years before the first cancer. Annual screening for uterine cancer is recommended beginning at the age 35 years. The method of screening include transvaginal ultrasound and hysteroscopy

**Prognosis** Coloscopy screening at 3 year intervals more than halves the risk of colorectal cancer, prevents colorectal cancer deaths, and decreases overall mortality by about 65% in HNPCC families

### Genes involved and Proteins

**Note** different genes can be respnsible for Lynch Syndrome:  
1) [hMSH2](#) (mutS (E. coli) homolog 2 (colon cancer, nonpolyposis type 1)) located in 2p22-p21  
2) [hMLH1](#) (mutL (E. coli) homolog 1 (colon cancer, nonpolyposis type 2)) located in 3p21.3

[hMSH6](#) (mutS (E. coli) homolog 6) located in 2p16  
[PMS2](#) (postmeiotic segregation increased (S. cerevisiae) 2) located in 7p22  
[PMS1](#) (postmeiotic segregation increased (S. cerevisiae) 1) located in 2q31.1  
[TGFβR2](#) (transforming growth factor, beta receptor II (70-80kD)) located in 3p22

## Protein

Localisation nuclear

Function These protein works on DNA mismatch repair pathways. hMSH21 et hMLH1 are similar to MutS andt MutL in Echerichia Coli. These two proteins participated to the recognition of DNA mismatch during DNA replication. They formed complex with hMSH3, hMSH6 and PMS2 allowing the mismatch repair

## Mutations

Germinal Yes; no mutations hot spot

Somatic Yes; extinction of hMLH1 by promoter hypermethylation

## External links

[OMIM](#) [120436](#)

[Orphanet](#) [Lynch Syndrome](#)

Association [Le syndrome HNPCC](#)

Registry <http://www.nfdht.nl/database/mdbchoice.htm>

## Bibliography

**Mutations predisposing to hereditary nonpolyposis colorectal cancer: database and results of a collaborative study. The International Collaborative Group on Hereditary Nonpolyposis Colorectal Cancer.**

Peltomaki P, Vasen HF.

Gastroenterology 1997; 113: 1146-58.

Medline [9322509](#)

**Controlled 15-year trial on screening for colorectal cancer in families with hereditary nonpolyposis colorectal cancer.**

Jarvinen HJ, Aarnio M, Mustonen H, Aktan-Collan K, Aaltonen LA, Peltomaki P, De La Chapelle A, Mecklin JP.

Gastroenterology 2000; 118: 829-34.

Medline [10784581](#)

**Incidence of hereditary nonpolyposis colorectal cancer and the feasibility of**

**molecular screening for the disease.**

Aaltonen LA, Salovaara R, Kristo P, Canzian F, Hemminki A, Peltomaki P, Chadwick RB, Kaariainen H, Eskelinen M, Jarvinen H, Mecklin JP, de la Chapelle A.

N Engl J Med 1998; 338: 1481- 1487.

Medline [9593786](#)

**Population-based molecular detection of hereditary nonpolyposis colorectal cancer`.**

Salovaara R, Loukola A, Kristo P, Kaariainen H, Ahtola H, Eskelinen M, Harkonen N, Julkunen R, Kangas E, Ojala S, Tulikoura J, Valkamo E, Jarvinen H, Mecklin JP, Aaltonen LA, de la Chapelle A.

J Clin Oncol 2000; 18: 2193-2200.

Medline [10829038](#)

[REVIEW articles](#)      *automatic search in PubMed*

[Last year publications](#)      *automatic search in PubMed*

**Contributor(s)**

Written      09-2001      Pierre Laurent-Puig

**Citation**

*This paper should be referenced as such :*

**Laurent-Puig P** . Hereditary non polyposis colorectal carcinoma (HNPCC Syndrome). Atlas Genet Cytogenet Oncol Haematol. September 2001 .  
URL : <http://AtlasGeneticsOncology.org/Kprones/HNPCC/LynchID10049.html>

© Atlas of Genetics and Cytogenetics in Oncology and Haematology

---