HEREDITARY CANCER SYNDROMES

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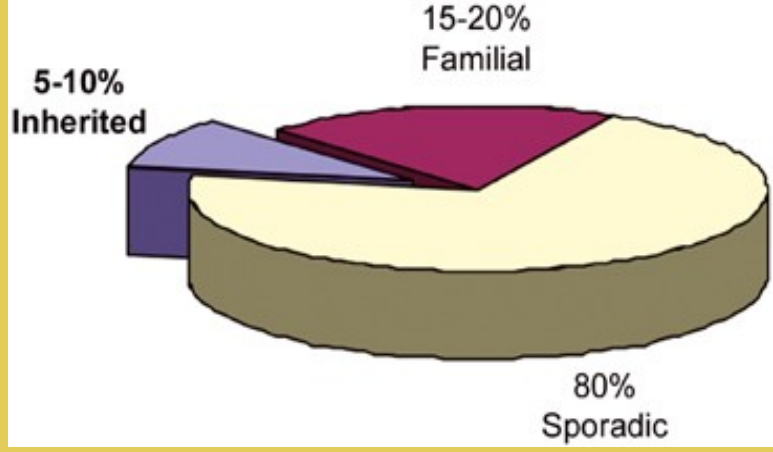
CONTENT

GENERAL



A hereditary cancer syndrome is a type of inherited disorder in which there's a higher than normal risk of certain types of cancer

Caused by mutations in certain genes passed from parent to child

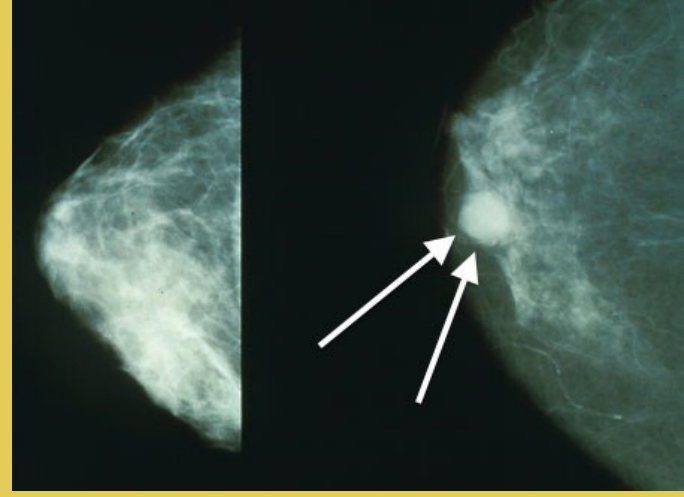
- Mutations: inherited x acquired (somatic)
- Most cancers are caused by acquired mutations

Cancer running in families due to similar behaviour x cancer running in families due to inherited genetic mutations

Pattern of cancer can be seen in families

- Several close family members with same type of cancer
- Cancer at early age
- Two or more cancer types in the same person

HEREDITARY BREAST AND OVARIAN CANCER SYNDROME



Due to autosomal-dominant inherited gene mutation in BRCA1 or BRCA2 genes

- Risk is higher with BRCA1 mutations
- Positive family history

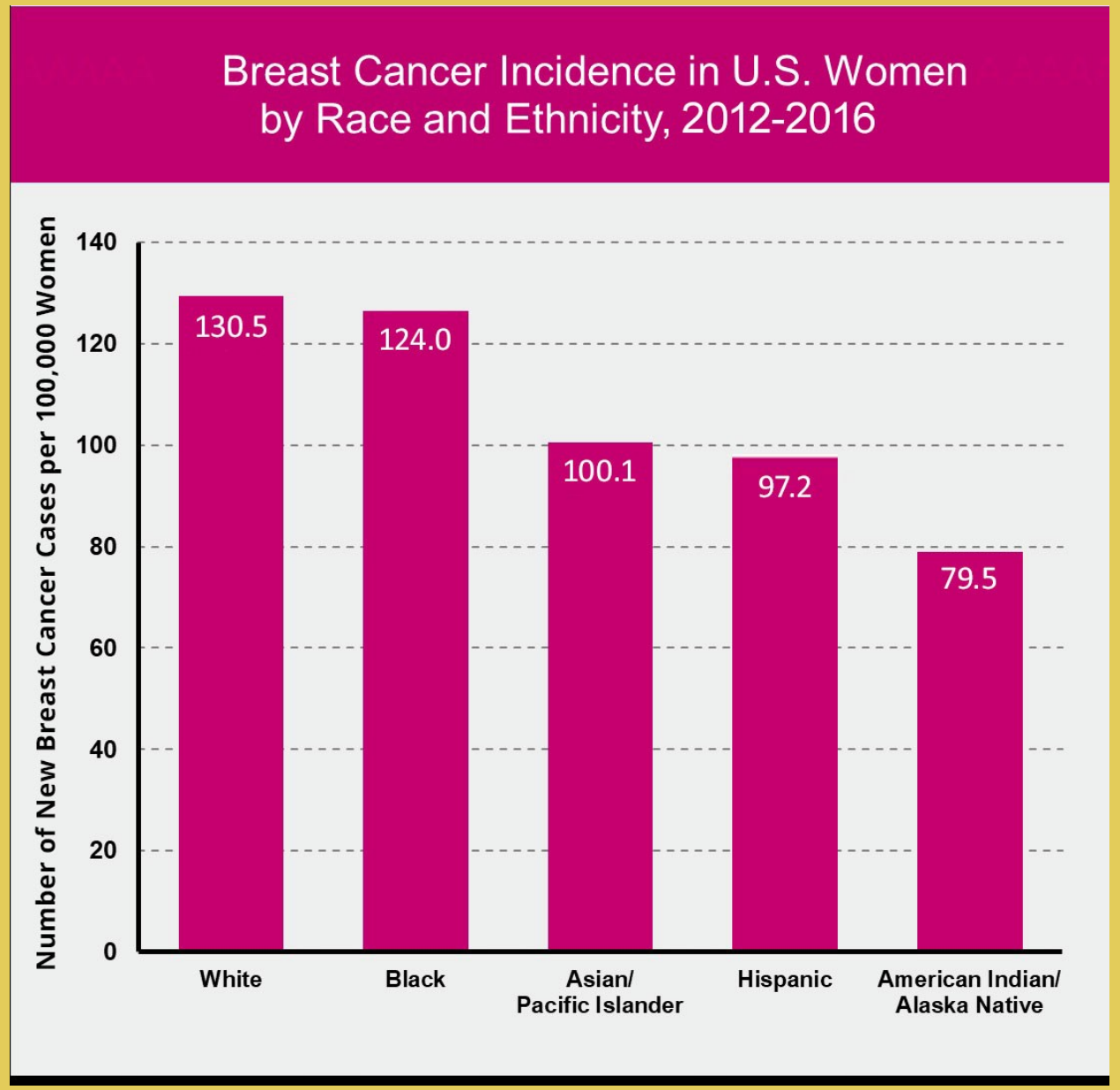
BRCA: tumour suppressor gene coding for a DNA repair protein

Increased risk of breast and ovarian cancer, and some other types like fallopian tube cancer, primary peritoneal cancer, male breast cancer etc.

Breast cancer is the most common malignancy in women

- BRCA mutation in 5-10% of all women with breast cancer

BRCA positive women develop breast cancer 15-20 years earlier than women without the mutation, bilateral breast cancer is more common in addition to other cancers subsequently


Breast Cancer Incidence in U.S. Women
by Race and Ethnicity, 2012-2016
Number of New Breast Cancer Cases per 100,000 Women
140
120
100
80
60
40
20
0
130.5
124.0
100.1
97.2
79.5
White
Black
Asian/
Pacific Islander
Hispanic
American Indian/
Alaska Native

LI-FRAUMENI SYNDRO

Autosomal-dominant mutation of p53 tumor suppressor g

Normally: p53 is expressed as a result of DNA damage → cell cycle

→ repair. DNA can't be fixed; Apoptosis of cell.

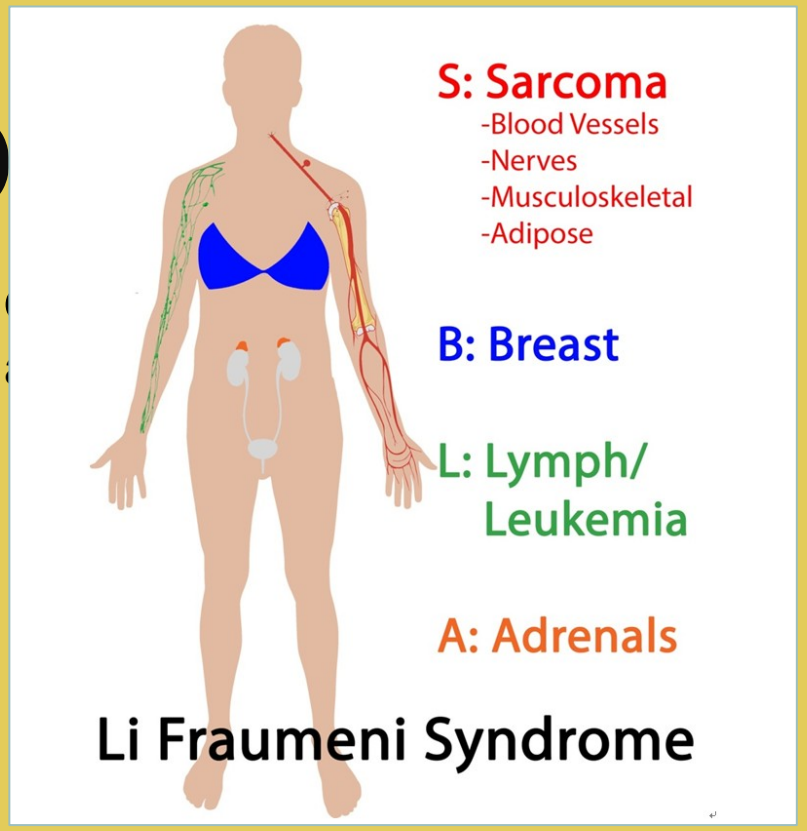
Predispose to cancer development

Presentation

Early cancer development

Variety of primary cancers in the same person

Development of multiple cancer types throughout life



Classical LFS malignancies: sarcoma, breast, brain and adrenal glands (80%)

Breast cancer is especially high risk → females have almost 100% lifetime risk of developing cancer

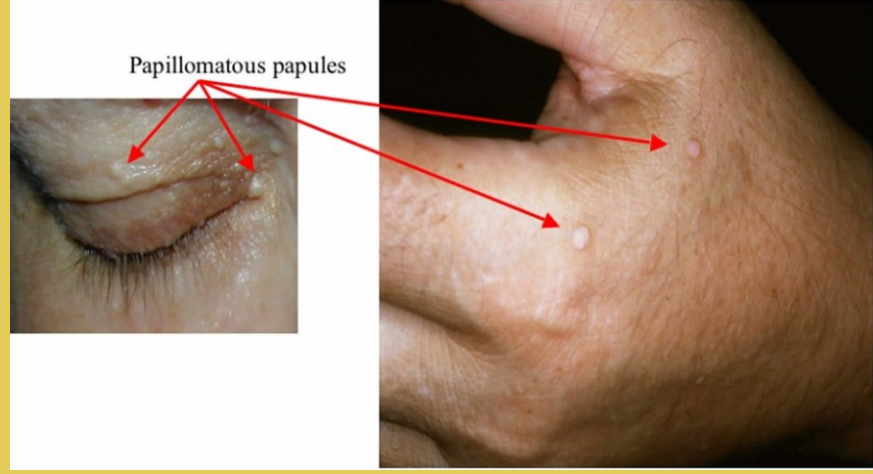
Males: 73% lifetime risk

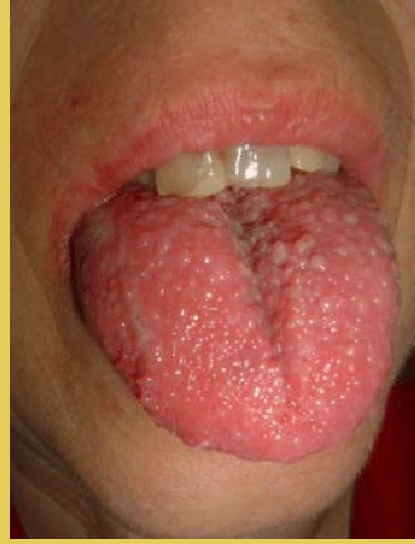
Risk of developing invasive cancer in LFS

By age 30: 50% in LFS, 1% in healthy person

By age 70: 90% in LFS, 18% in healthy person

COWDEN SYNDROME





Also known as multiple hamartoma syndrome

Autosomal dominant mutation of tumour suppressor gene PTEN

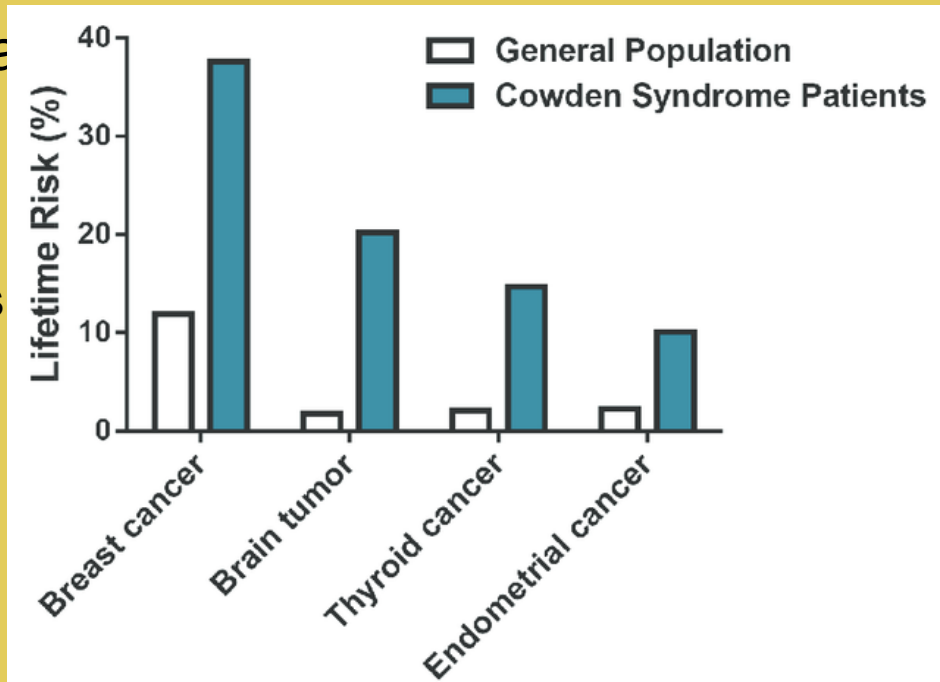
- PTEN gene negatively regulates receptor tyrosine kinase pathway and facilitate repair of DNA errors

Characterized by multiple overgrowths of hamartoma

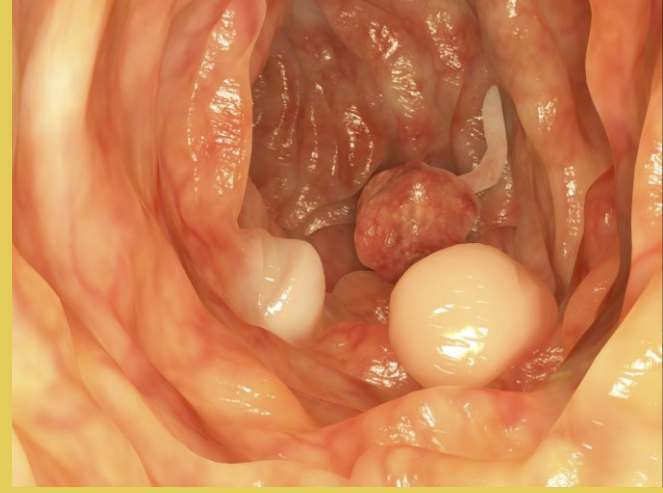
- Multiple GI polyps
- Skin and mucous membranes: papules, hyperkeratosis
- Thyroid disorders in >50% (multinodular goiter, adenoma)
- Benign breast disorders: fibroadenomas, intraductal papillomas

Associated malignancies:

- breast adenocarcinoma,
- thyroid adenocarcinoma,
- skin SCC



LYNCH SYNDROME



Hereditary nonpolyposis colorectal cancer

Autosomal dominant mutation in mismatch repair genes (varying penetrance)

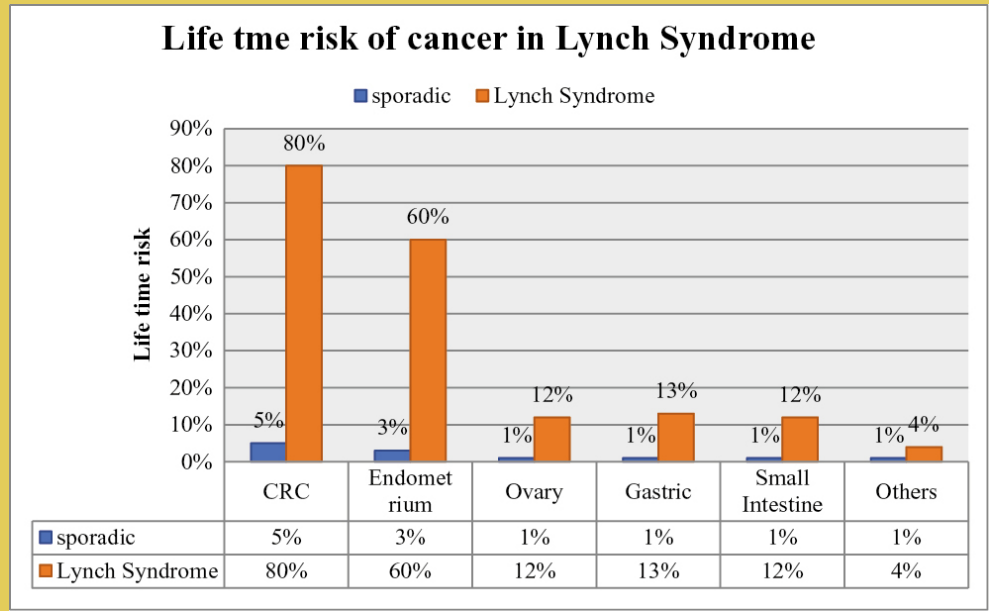
Associated with higher risk of colorectal, gastric and endometrial cancer

- Most common cause of inherited CRC

Development of a small number of colonic adenomas with a significant risk of malignant change

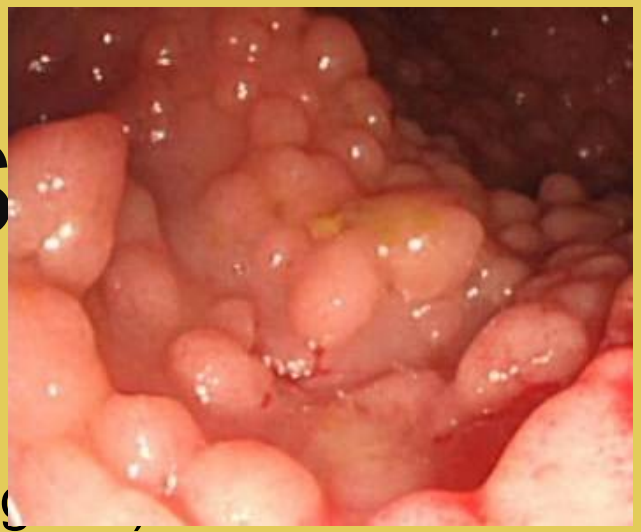
70-80% lifetime risk of developing CRC

- Average onset: 44 years old
- Patients are often asymptomatic until they present with symptoms of advanced cancer



	CRC	Endometrium	Ovary	Gastric	Small Intestine	Others
sporadic	5%	3%	1%	1%	1%	1%
Lynch Syndrome	80%	60%	12%	13%	12%	4%

FAMILIAL ADENOMATOUS POLYPOSIS



Autosomal dominant mutation of APC gene (tumour suppressor g

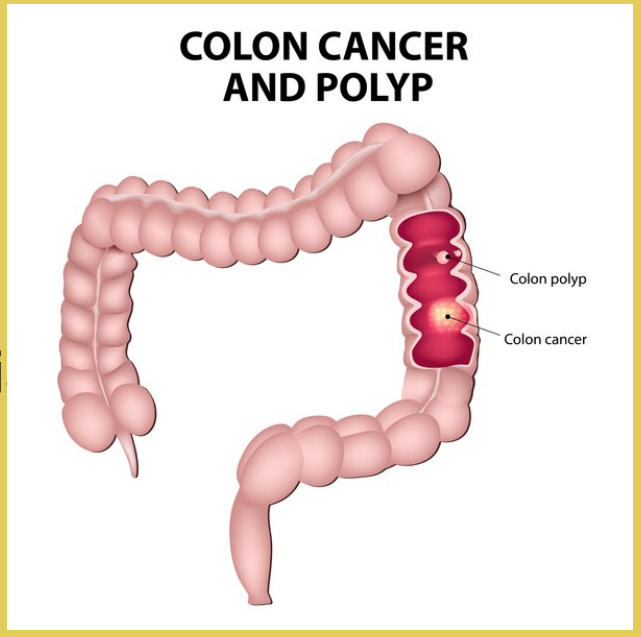
Characterized by formation of a high number of adenomatous polps in the epithelium of large intestine

- Initially asymptomatic until it progresses to colon cancer
- 100% risk of colorectal cancer by age of 45

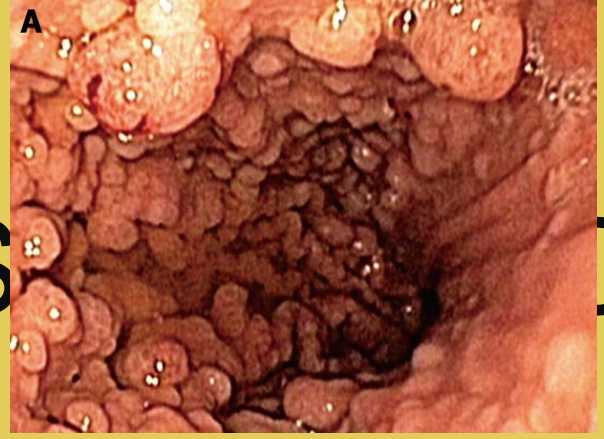
1:10 000-30 000 live births, M = F

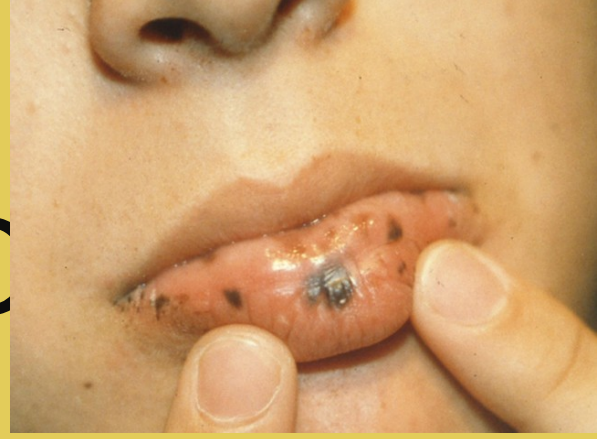
Variants

- Attenuated FAP: 10-100 polyps only, later onset of CA
- Gardner syndrome: FAP + extracolonic tumours (bone, soft ti
- Turcot syndrome: FAP + brain tumours



PEUTZ-JEGHERS





Autosomal dominant genetic disorder, meaning that anyone with it has a 50% chance of passing it to their offsprings.

Characterized by:

- Benign hamartomatous polyps in the GIT
- Hyperpigmented macules in the lips and oral mucosa (melanosis)

A gene is associated with the mutation. On chromosome 19, the STK11 gene, a tumor supressor gene.

Patients have increased risk for carcinomas of the lungs, breasts, liver, ovaries, uterus, testes…