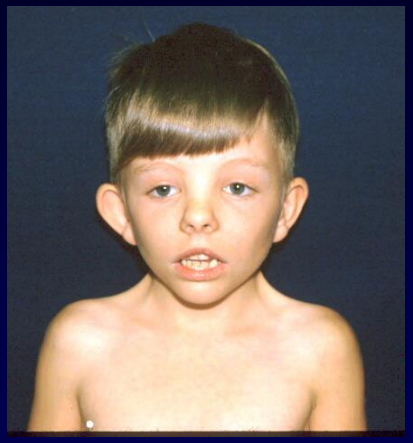
History of Turner and Noonan Syndromes

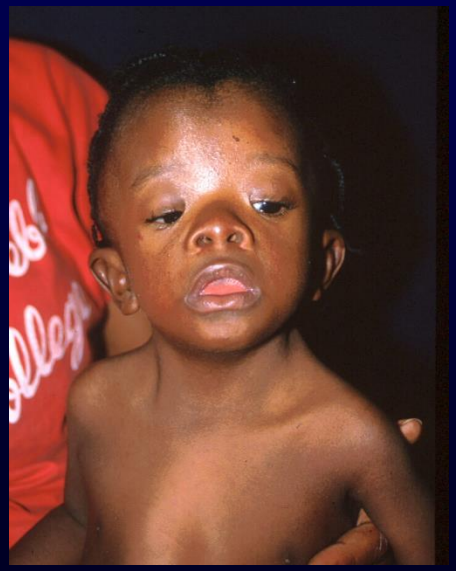
Noonan Syndrome	Turner Syndrome
Jacquelin Noonan, 1962	Giles Turner, 1958
Web neck	Web neck
Low-set ears	Low-set ears
Pedal edema +	Pedal edema ++
Wide-spaced nipples	Wide-spaced nipples
Short stature +	Short stature ++
CHD (right sided)	CHD (left sided)
Both sexes, nl chromosomes	Females only: 45,X
15% familial (dominant)	Not inherited
Subnormal intelligence	Normal intelligence
Normal fertility	1^0 amenorrhea

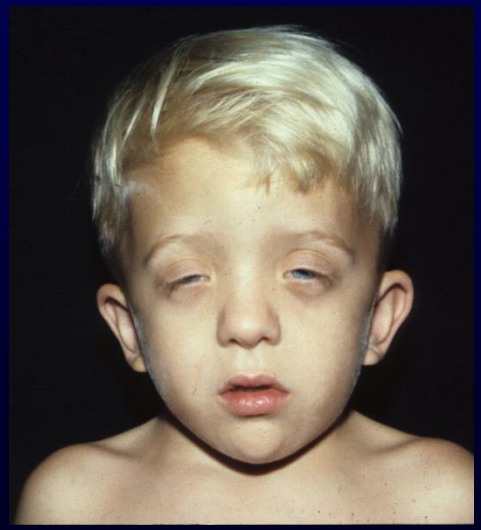


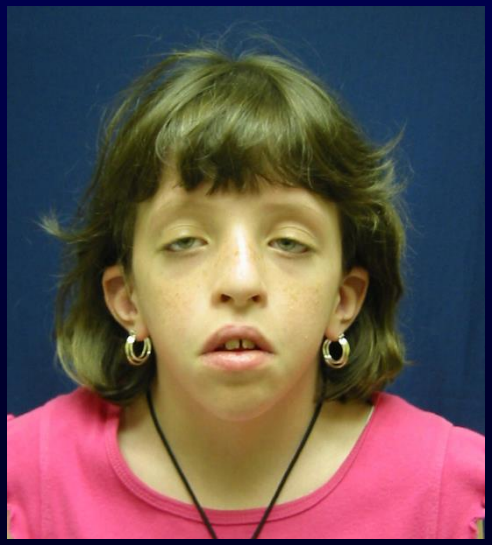
Noonan Syndrome

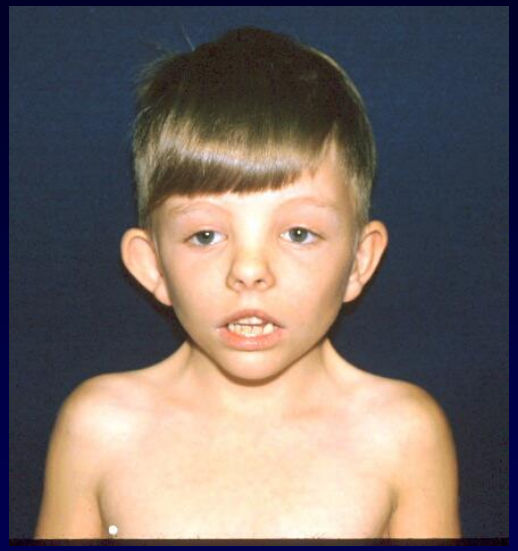
- Webbed neck, neonatal lymphedema
- Pulmonary valve stenosis
- Wide spaced nipples, pectus
- Low set ears, downslanted eyelids with ptosis
- Learning delay
- Etiology: RAS-MAPK signal transduction path
  - PTPN11 (50% have mutations). Other genes include: KRAS, SOS1, RAF1, SHOC2, NRAS and others

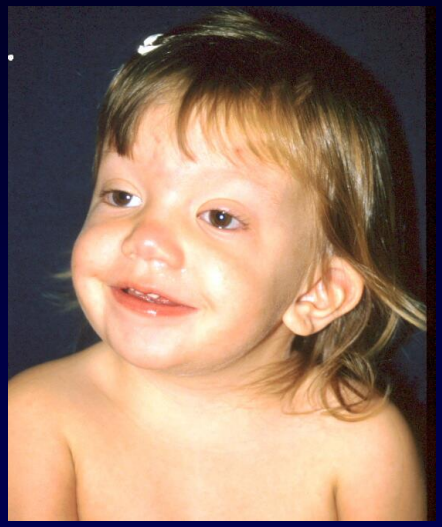
Individuals with the Noonan syndrome

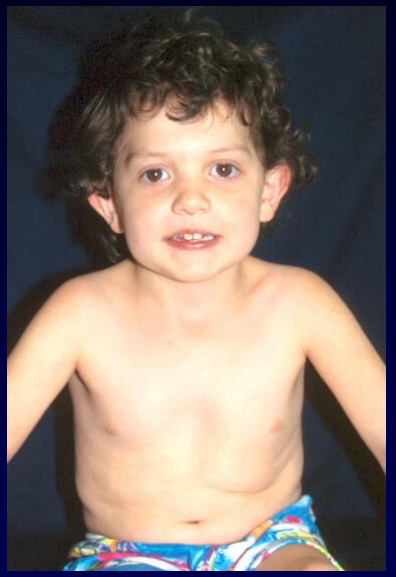








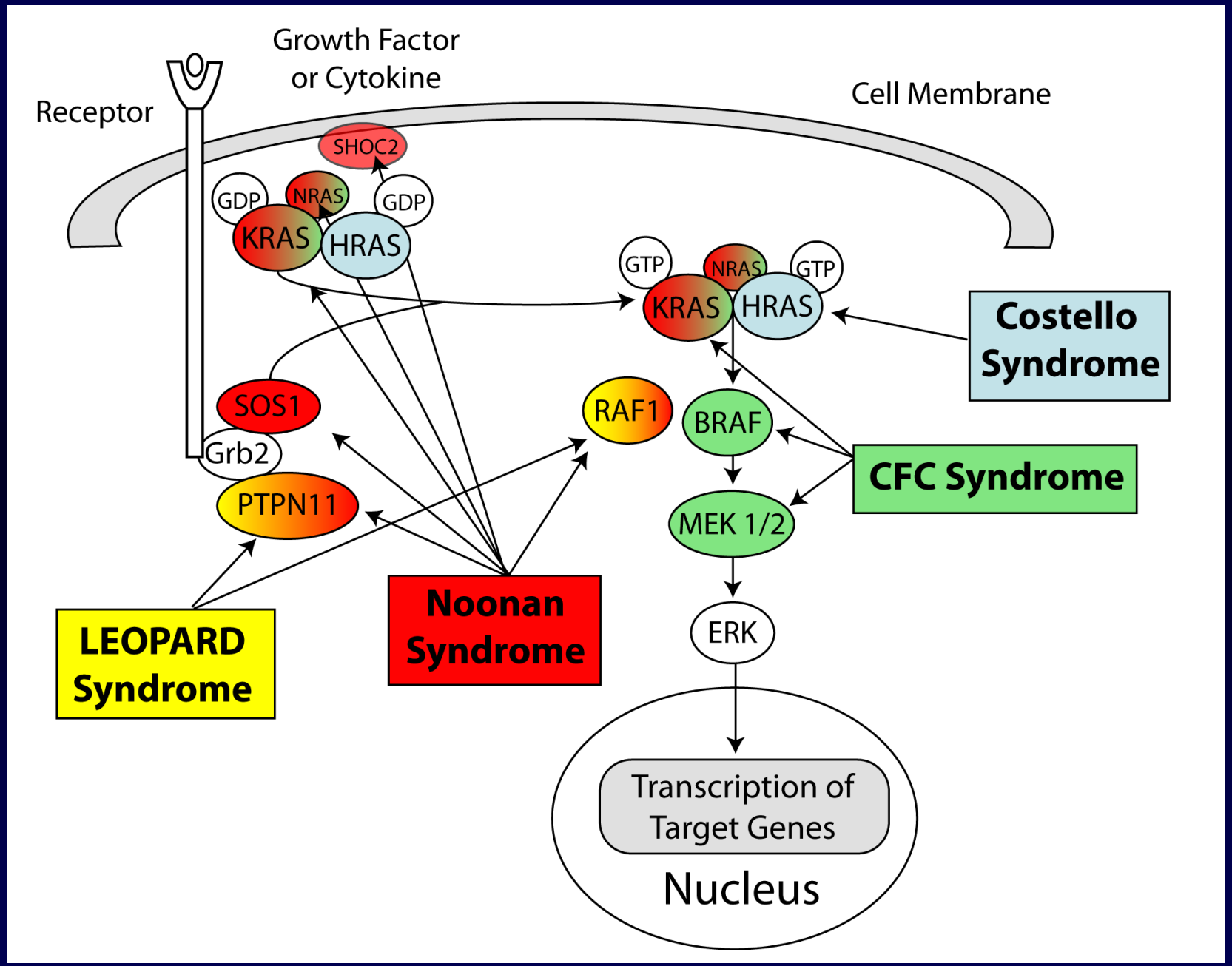




Noonan Syndrome and Related Conditions

- Related genes with proteins involved in common signaling pathway
- May be grouped as the “Noonan-phenotype” conditions
- Syndromes:
  - Noonan
  - Cutaneous-Cardio-Facial (CFC)
  - Costello
  - LEOPARD

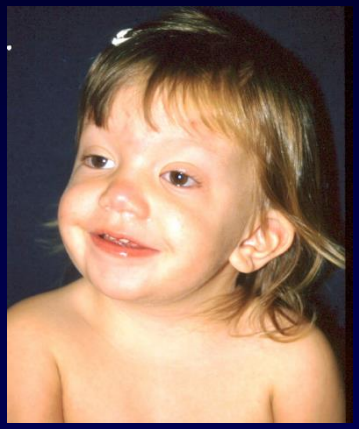
Example of some of the genes that can cause the Noonan phenotype



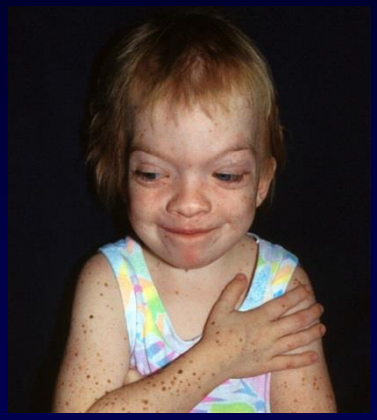
- Cardio-Facial-Cutaneous (CFC)
  - Sparse, wooly hair
  - Hyperkeratotic, scaly skin

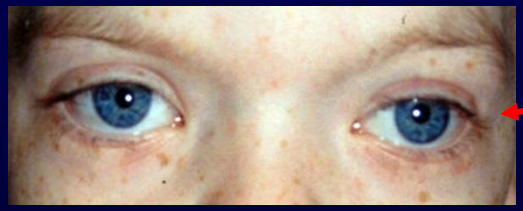
- Costello
  - Coarse face
  - relative/absolute macrocephaly
  - Tumor predisposition

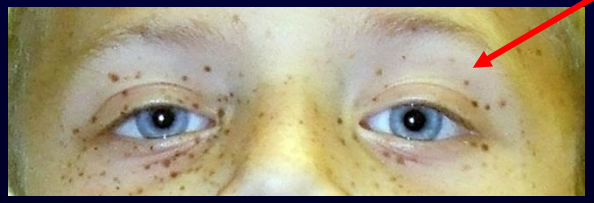
- **Noonan Phenotype Core Features**
  - **Craniofacial**
  - **Cardiovascular**
  - **Developmental**

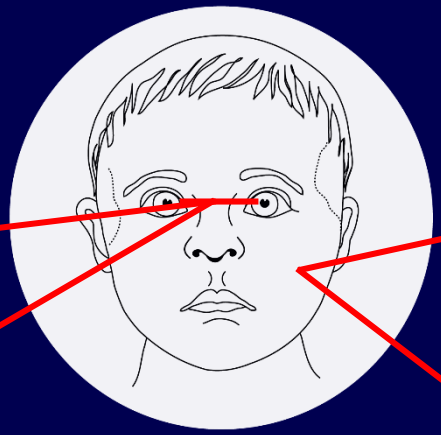


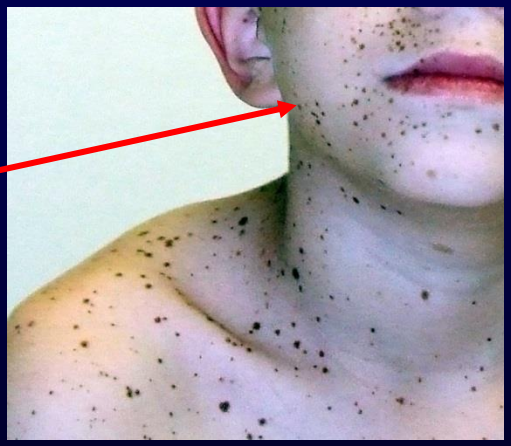
- LEOPARD
  - Lentigenes, nevi
  - Hearing loss
  - Leftward QRS axis

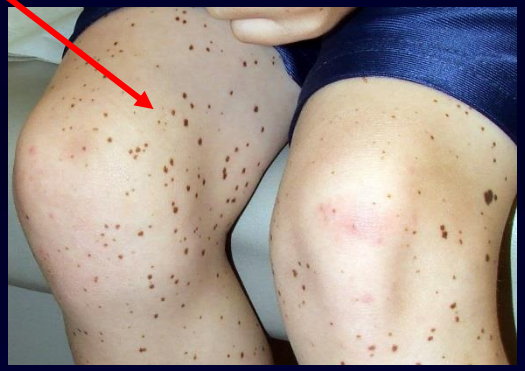






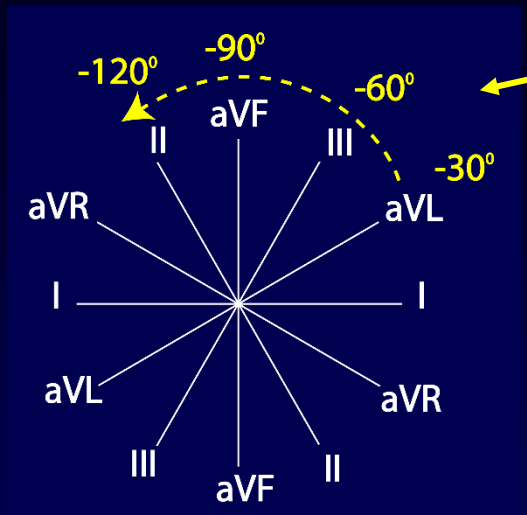






LEOPARD Syndrome

- Lentigines
- EKG abnormalities
- Ocular hypertelorism
- Pulmonic stenosis
- Abnormalities of genitalia
- Retardation of growth
- Deafness



Left axis deviation