




**Rolling the DICER1**

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**Financial Disclosure**

Ann & Robert H. Lurie  
Children's Hospital of Chicago

- Shelly McQuaid and Barbara Lockart do not have any actual or potential conflicts of interest to report
- No off label medication uses will be discussed

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**Learning Outcomes**

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- The learner will be able to identify benign and malignant conditions suggestive of DICER1 mutations.
- The learner will demonstrate increased knowledge of patient and family histories concerning for DICER1 mutation, as well as recommendations for genetic counseling and screening and the ethics of genetic testing.

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## After the shock . . .

- Comes the doubt
- And then the questions



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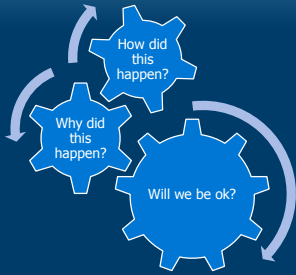
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A wise nursing instructor once told me,  
 "Everything is genetic . . .  
 but not everything genetic is hereditary."



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How do the genetic pieces fit together?



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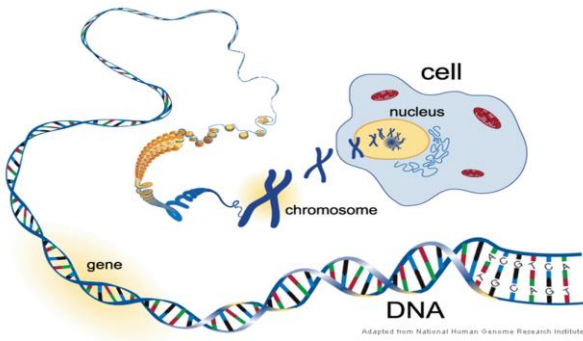
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Adapted from National Human Genome Research Institute

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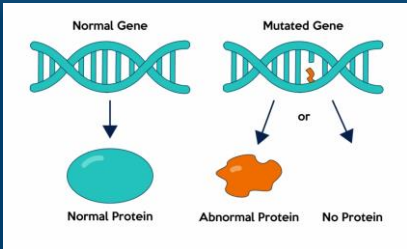
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## DICER1 (Familial Pleuropulmonary Blastoma Tumor Predisposition)

- Pleuropulmonary Blastoma (PPB)
- Cystic Nephroma
- Ovarian Sertoli-Leydig cell tumor
- Embryonal Rhabdomyosarcoma
- Intraocular Medulloepithelioma
- Supratentorial primitive neuroectodermal tumor
- Multinodular goiter
- Others: Pituitary Blastoma, Pineoblastoma

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**Table 1. Key clinical phenotypes associated with germline DICER1 pathogenic variants**

Phenotype and relative frequency	Approximate age of susceptibility range (years)	Malignant (M) or benign (B)	Deaths associated in DICER1-related cases
<b>Most frequent phenotypes</b>			
PPB			
Type I (cystic) PPB	0-24 m (8 m)	M	y, if progression to type I or II
Type II (cystic) PPB	12-60 m (21 m)	M	y, ~40%
Type III (solid) PPB	38-72 m (64 m)	M	y, ~80%
Type IV (cystic) PPB	Any age	B or M	Note observed
Multinodular goiter*	2-40 y (10-20 y)	B	n
Cystic nephroma	0-48 m (undetermined)	B	n (one anaplastic sarcoma of kidney before)
Sarcoma/lymphoma of testis of ovary	2-40 y (10-25 y)	M	y, ~45% of cases
<b>Moderate frequency phenotypes</b>			
Cervix embryonal rhabdomyosarcoma	4-45 y (10-20 y)	M	Note observed
<b>Rare frequency phenotypes</b>			
ZTC	5-40 y (10-20 y)	M	Note observed
Olfact. tumor	3-55 y (undetermined)	M	Note observed
Juvenile hamartomatous intestinal polyps	0-4 y (undetermined)	B	n
Ovary/ovary medulloepithelioma	2-10 y (undetermined)	B or M	Note observed
Neural chondrosarcoma/nerve sheath tumor	0-8 y (undetermined)	B	n
Pituitary blastoma	0-24 m (undetermined)	Undetermined	y, ~50%
Pineoblastoma	2-25 y (undetermined)	M	y
<b>Very rare phenotypes</b>			
Neoplastic carcinoma of kidney	Estimated 2-20 y	M	y
Medulloblastoma	Undetermined	M	Unknown
EMMS bladder	Estimated <1 y	M	Note observed
EMMS ovary	Undetermined	M	Note observed
Medulloepithelioma	Estimated <1 y	M	y
Congenital ptosis oculi	Birth	B	n
Juvenile phalloid of tumor	Undetermined	M	Note observed
Supraorbital tumor	Undetermined	M	Note observed
Cervix immature neuroectodermal tumor	Undetermined	M	Note observed

Schultz KA et al. Clin Cancer Res; 2017; 23(2)

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## DICER1 Management

- Chest CT at 3-6 months of age
  - If normal, follow-up image at 2.5-3 years of age.
  - Consider every 6 months screening until 8 years and annual from 8-12 years.
- Biannual abdominal ultrasound until age 8 and annually thereafter
  - Gonadal tumors have been reported into the 40s.
- Consider screening brain MRI
  - Risk-benefit ratio is currently unknown.

Schultz KA et al. Clin Cancer Res; 2017; 23(12)

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### Cancer Genetic Testing in Children

"The decision as to whether to pursue clinical genetic testing for hereditary cancer predisposition for children should always be guided by **the best interest of the child.**"

- Childhood-onset disease?
- Effective interventions?
- Can genetic test results be adequately interpreted?

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### Testing Benefits

### Testing Challenges

- Can guide disease management and allow for initiation of surveillance for second primary cancers
  - Can identify children at increased risk, allowing for education, surveillance and possible behavioral modification
    - Can also eliminate surveillance needs for individuals who do not have genetic abnormality
- Timing
  - Understanding and recommendations evolve as science advances
  - Child's age, maturity, and cognitive ability, family culture
  - Assent of minor child

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### Long-term issues

- Transitioning patient to adult health care team
- Assisting adolescents and young adults with establishing autonomy over health
- Monitoring for late-effects
  - Multiple therapies and risk of late-effects from cancer treatment
- Genetic counseling as patient matures
  - Families struggle with developmentally appropriate information
- Reproductive health
- Mental health

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### Nursing Interventions

- Listening
  - Family history
- Questioning
  - How does this all fit together?
- Referring to colleagues in cancer pre-disposition clinic
  - At home institution or pediatric center
  - NIH
- Referring to child life, psycho-social team, chaplain services, school liaison, and family support services
  - Cancer affects the entire family

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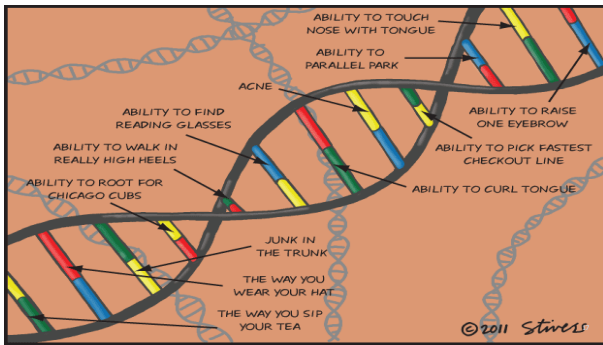
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### Questions?

*Thank you*

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### Resources

- International Pleuropulmonary Blastoma/DICER1 Registry  
<https://www.ppbregistry.org/>
- International Ovarian and Testicular Stromal Tumor Registry  
<https://www.otstregistry.org/>
- National Library of Medicine Genetics Home Reference  
<https://ghr.nlm.nih.gov/condition/dicer1-syndrome>

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