OMICS and AI in PEDIATRICS

Omics driven systemic treatments

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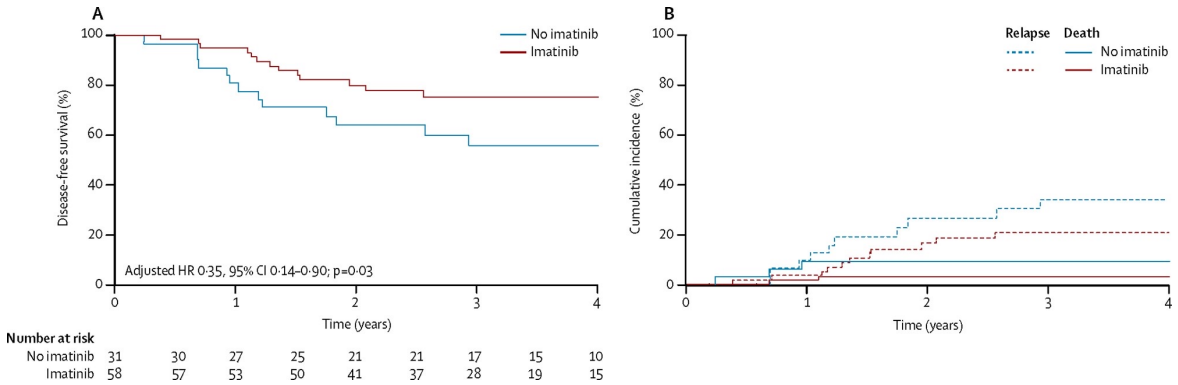
Neuro-oncology Unit

19 October 2022

Omics-driven approach for pediatric cancer

- Imatinib after induction for treatment of children and adolescents with Philadelphia-chromosome-positive acute lymphoblastic leukemia (EsPhALL)
  - a randomized, open-label, intergroup study



Lancet Oncol. 2012 Sep;13(9):936-45.

Marketing approval for adults in 2006; for children in 2013

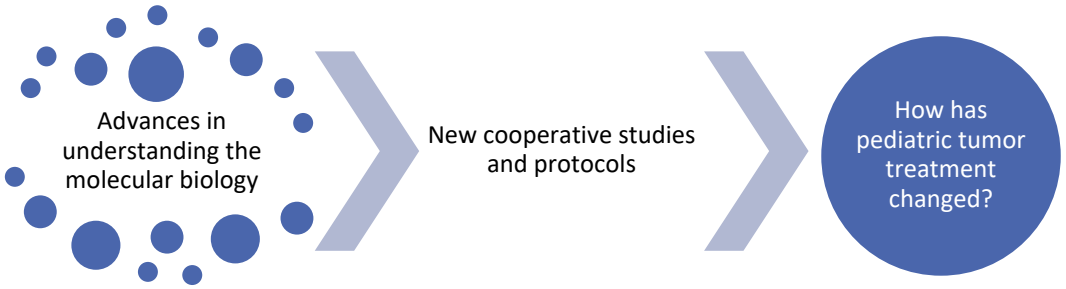
Being a pediatric oncologist in 2022 means

- Improve Survival
- Improve the quality of life
- Improve knowledge and research

WHO Classification of Pediatric Tumors: from the Optical into the Molecular Era

Pediatric tumors are fundamentally different from ones occurring in adults

- Tumor types, molecular characteristics, and pathogenesis are unique, often originating from a single genetic driver event
- The specific diagnostic challenges of childhood tumors led to the development of the first World Health Organization (WHO) Classification of Pediatric Tumors. The classification is rooted in a multilayered approach, incorporating morphology, IHC, and molecular characteristics.



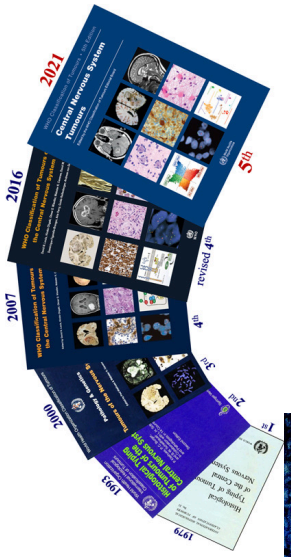
Cancer Discov (2022) 12 (2): 331–355.

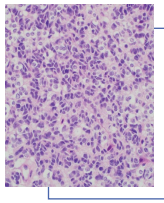
Journal of Neuropathology and Experimental Neurology
Vol. 61, No. 3
March, 2002
pp. 215–225

The WHO Classification of Tumors of the Nervous System

PAUL KLEIHUES, MD, DAVID N. LOUIS, MD, BERND W. SCHEITHAUER, MD, LUCY B. RORKE, MD,
GUIDO REIFENBERGER, MD, PHD, PETER C. BURGER, MD, AND WEBSTER K. CAVENEE, PHD

In the past we had few old principles…

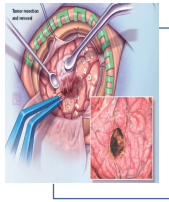




Embryonal tumor

- Radiotherapy and chemotherapy

No radiotherapy in children < 3 years

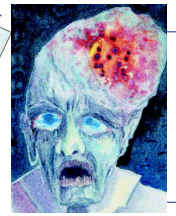


Low grade glioma

- Surgical disease

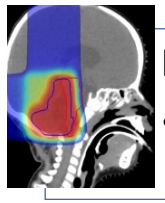
Chemosensitivity

- Medulloblastoma: Platinum-based drugs



High grade glioma

- Incurable



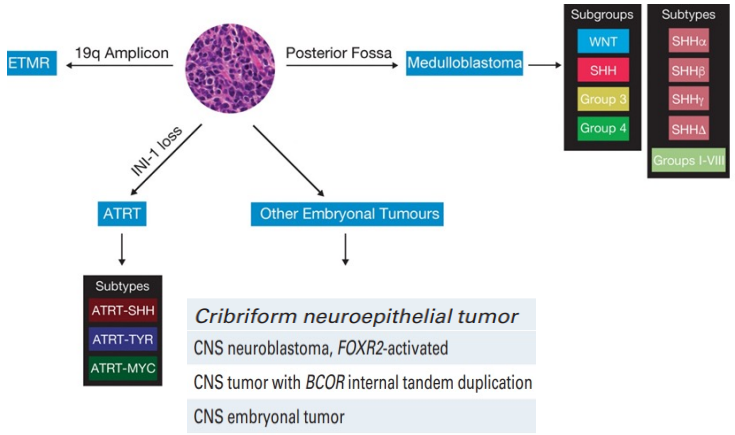
Radiosensitivity

- Ependymoma

Tumors of Neuroepithelial Tissue

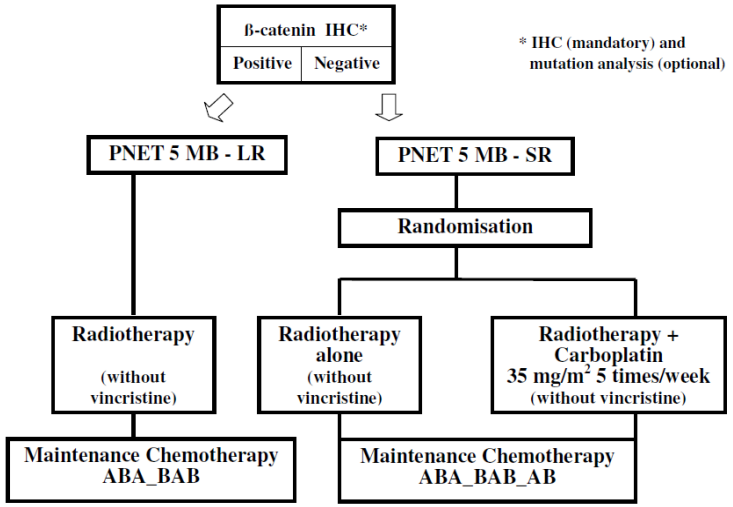
Astrocytic tumors	
Diffuse astrocytoma	9400/3[1]
Fibrillary astrocytoma	9420/3
Protoplasmic astrocytoma	9410/3
Gemistocytic astrocytoma	9411/3
Anaplastic astrocytoma	9401/3
Glioblastoma	9440/3
Giant cell glioblastoma	9441/3
Gliosarcoma	9442/3
Pilocytic astrocytoma	9421/1
Pleomorphic xanthoastrocytoma	9424/3
Subependymal giant cell astrocytoma	9384/1
Oligodendroglial tumors	
Oligodendroglioma	9450/3
Anaplastic oligodendroglioma	9451/3
Mixed gliomas	
Oligoastrocytoma	9382/3
Anaplastic oligoastrocytoma	9382/3
Ependymal tumors	
Ependymoma	9391/3
Cellular	9391/3
Papillary	9393/3
Clear cell	9391/3
Tanycytic	9391/3
Anaplastic ependymoma	9392/3
Myxopapillary ependymoma	9394/1
Subependymoma	9383/1
Choroid plexus tumors	
Choroid plexus papilloma	9390/0
Choroid plexus carcinoma	9390/3
Glial tumors of uncertain origin	
Astroblastoma	9430/3
Gliomatosis cerebri	9381/3
Chordoid glioma of the 3rd ventricle	9444/1
Neuronal and mixed neuronal-glial tumors	
Gangliocytoma	9492/0
Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos)	9493/0
Desmoplastic infantile astrocytoma/ganglioglioma	9412/1
Dysembryoplastic neuroepithelial tumor	9413/0
Ganglioglioma	9505/1
Anaplastic ganglioglioma	9505/3
Central neurocytoma	9506/1
Cerebellar liponeurocytoma	9506/1
Paraganglioma of the filum terminale	8680/1
Neuroblastic tumors	
Olfactory neuroblastoma (Aesthesioneuroblastoma)	9522/3
Olfactory neuroepithelioma	9523/3
Neuroblastomas of the adrenal gland and sympathetic nervous system	9500/3
Pineal parenchymal tumors	
Pineocytoma	9361/1
Pineoblastoma	9362/3
Pineal parenchymal tumor of intermediate differentiation	9362/3
Embryonal tumors	
Medulloepithelioma	9501/3
Ependymoblastoma	9392/3
Medulloblastoma	9470/3
Desmoplastic medulloblastoma	9471/3
Large cell medulloblastoma	9474/3
Medullomyoblastoma	9472/3
Melanotic medulloblastoma	9470/3
Supratentorial primitive neuroectodermal tumor (PNET)	9473/3
Neuroblastoma	9500/3
Ganglioneuroblastoma	9490/3
Atypical teratoid/rhabdoid tumor	9508/3

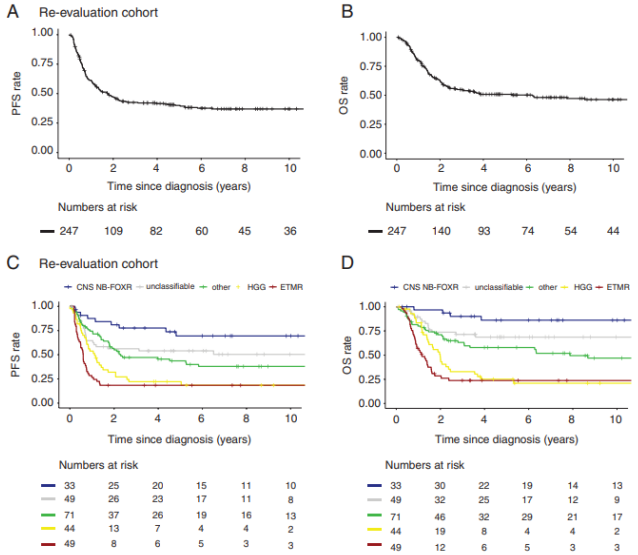
Embryonal tumors – exPNET: thime to rethinking the role of radiation



Adapted from: The Journal of Pathology, Volume: 251, Issue: 3, Pages: 249-261, 11 May 2020

SIOP E PNET 5 protocol





Neuro-Oncology

23(9), 1597–1611, 2021 | doi:10.1093/neuonc/noab136 | Advance Access date 2 June 2021

Therapeutic implications of improved molecular diagnostics for rare CNS embryonal tumor entities: results of an international, retrospective study

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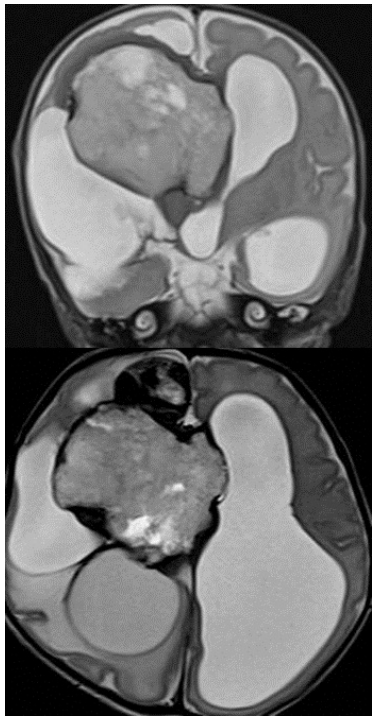
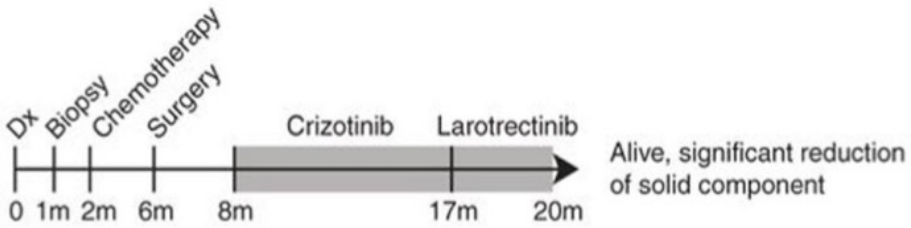
MODERN RADIATION ONCOLOGY

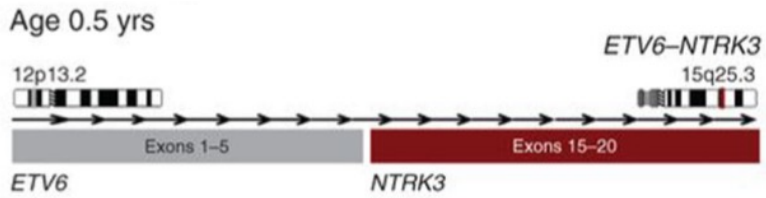
Infant-type hemispheric glioma: time to rethinking the role of chemo

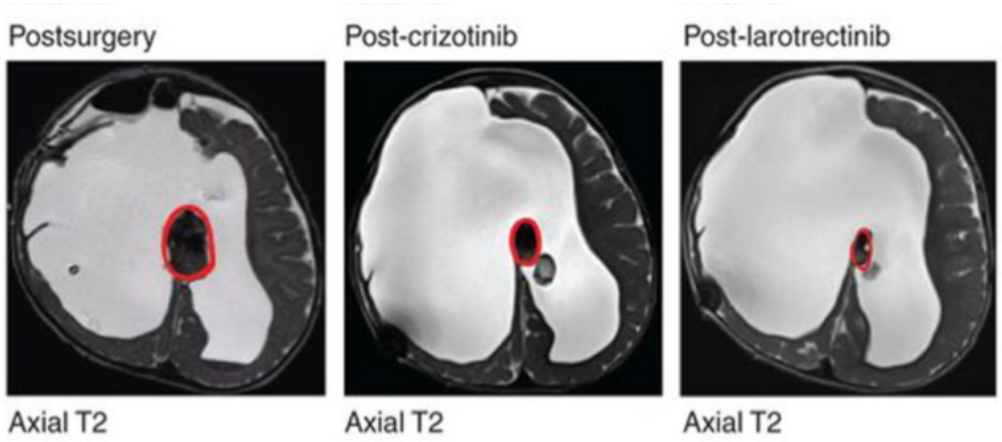


Nicole

1-day of life, 2017

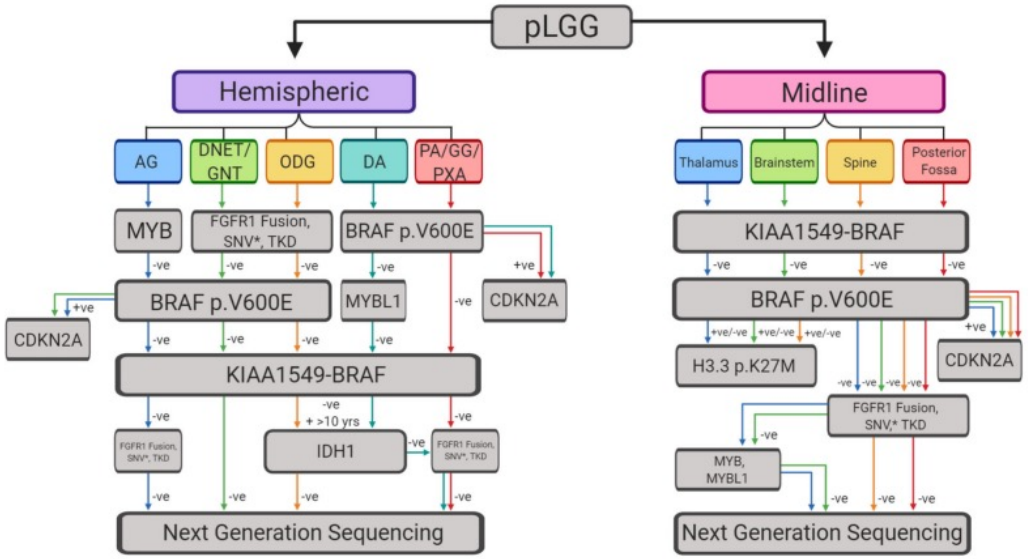




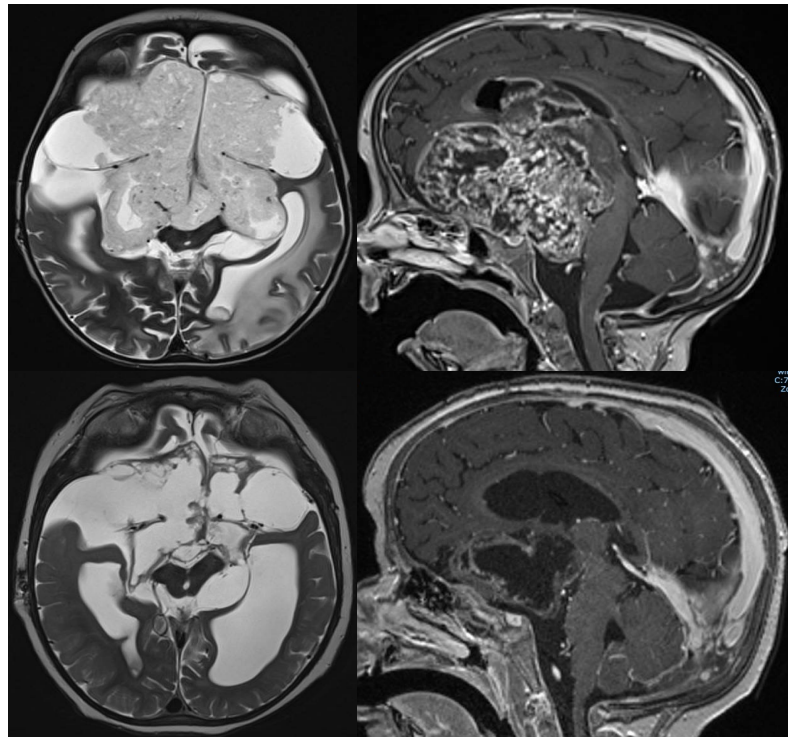


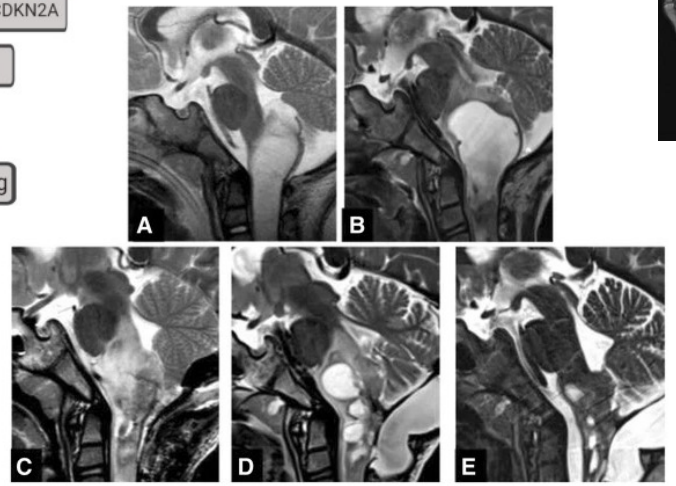
Cancer Discov. 2020 July ; 10(7): 942–963

Pediatric low-grade glioma: time to rethink the role of surgery?



KIAA1549-BRAF fusion



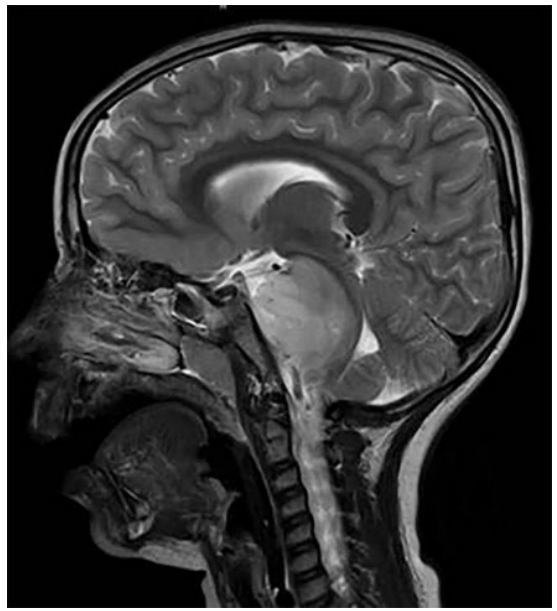


BRAFv600E mutation

Ryall et al. Acta Neuropathologica Communications (2020)

J Transl Med. 2014 Dec 19;12:356

DMG: time to rethink a lot of things…

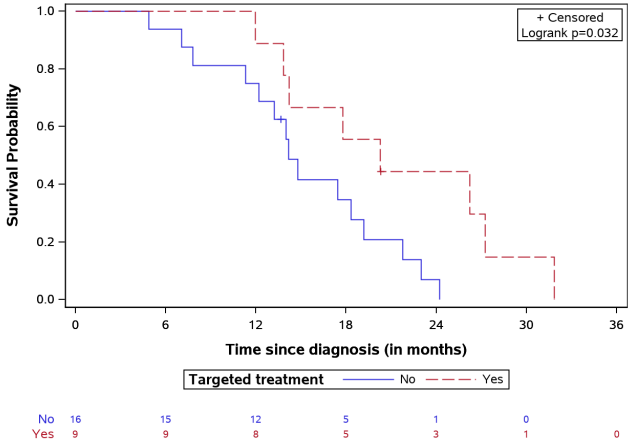


Targeted therapy for pediatric diffuse intrinsic pontine glioma: a single-center experience

Ther Adv Med Oncol
2022, Vol. 14: 1–19
DOI: 10.1177/17588359221113693

Giada Del Baldo, Andrea Carai, Rachid Abbas, Antonella Cacchione, Mara Vinci, Valentina Di Ruscio, Giovanna Stefania Colafati, Sabrina Rossi, Francesca Diomedi Camassei, Nicola Maestro, Sara Temelso, Giulia Pericoli, Emmanuel De Billy, Isabella Giovannoni, Alessia Carboni, Martina Rinelli, Emanuele Agolini, Alan Mackay, Chris Jones, Silvia Chiesa, Mario Balducci, Franco Locatelli* and Angela Mastronuzzi*

Bambino Gesù OSPEDALE PEDIATRICO



The median OS time was longer in the targeted treatment group, reaching 20.26 months [IQR: 14.21– 27.25] versus 14.18 months
[IQR: 11.76–19.19] for the non-targeted treatment group, p = 0.032.

We detected targetable alterations in 15/25 patients (60%) including:

- mTOR/pmTOR (71%)
- ACVR1 (33.3%)
- BRAFv600E (7%)
- PDGFRA (9%)

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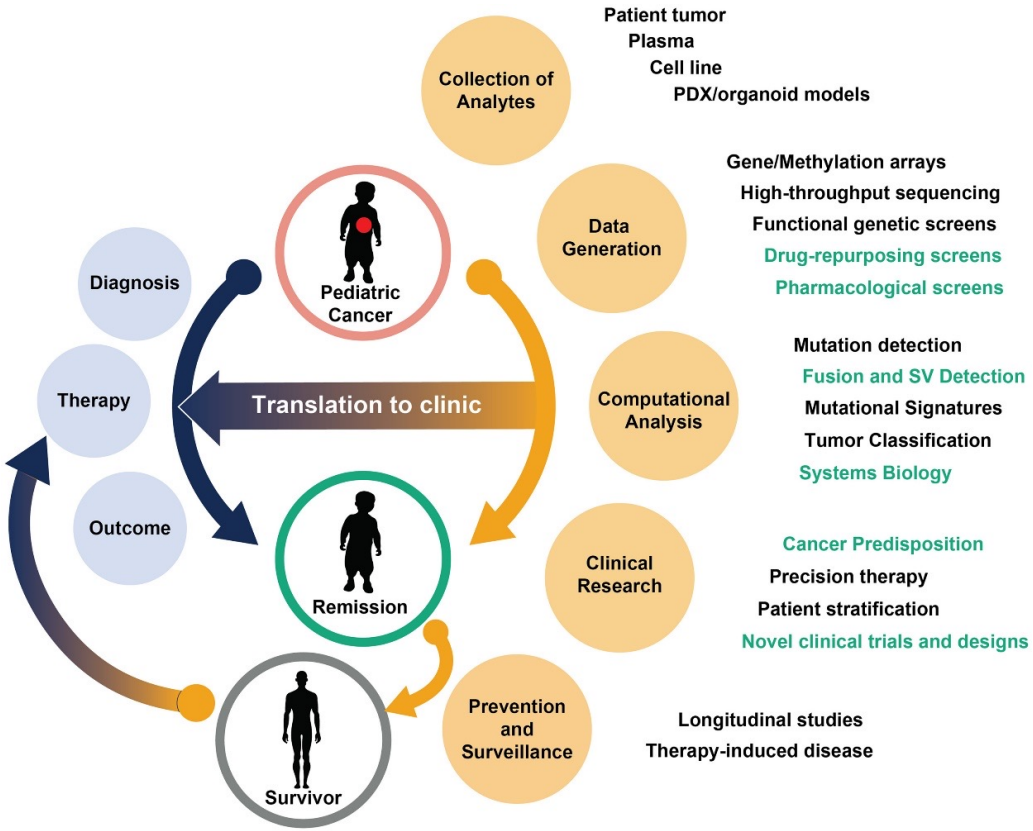
Conclusions: the future is now



Biochim Biophys Acta Rev Cancer. 2021;1876(1):188571.

Thank you for your attention

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