SBGN Pathway of the Month

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University of Southern California

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Challenges to represent biological pathways with SBGN

Leading Edge
Review

Cell

Lessons from the Cancer Genome

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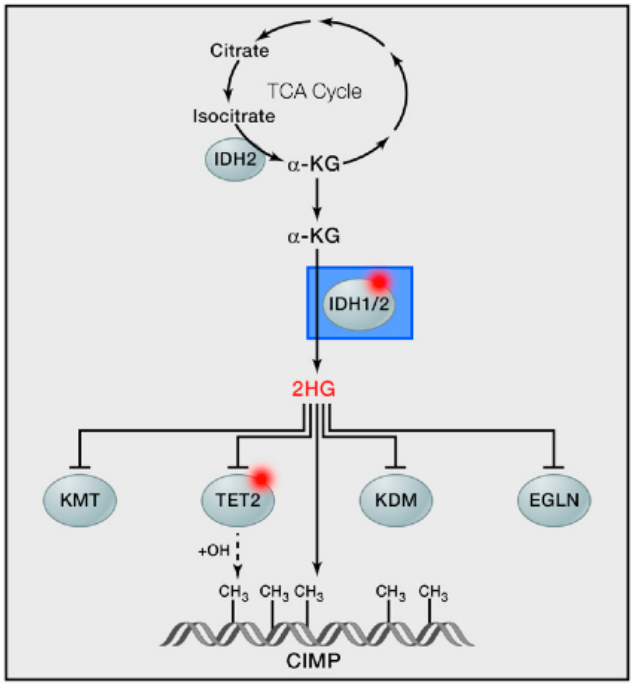
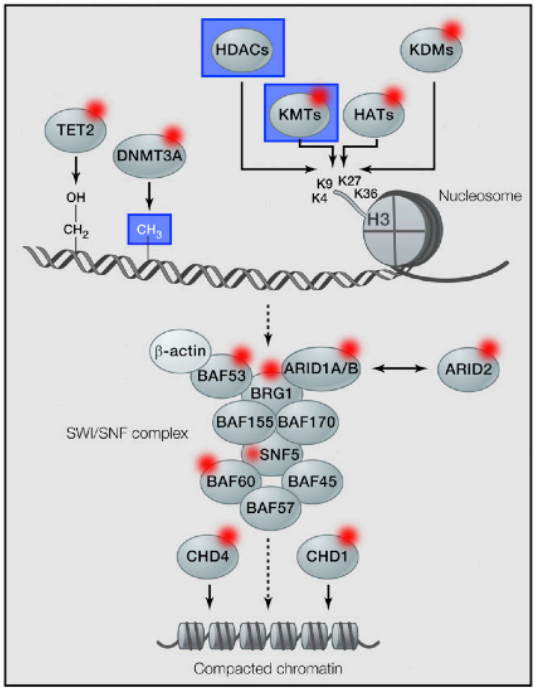
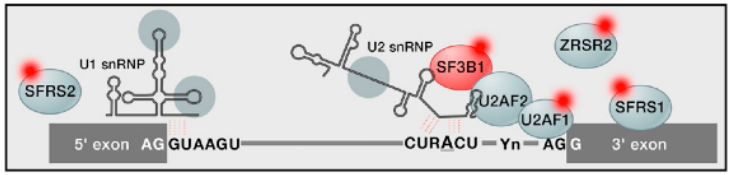
http://dx.doi.org/10.1016/j.cell.2013.03.002

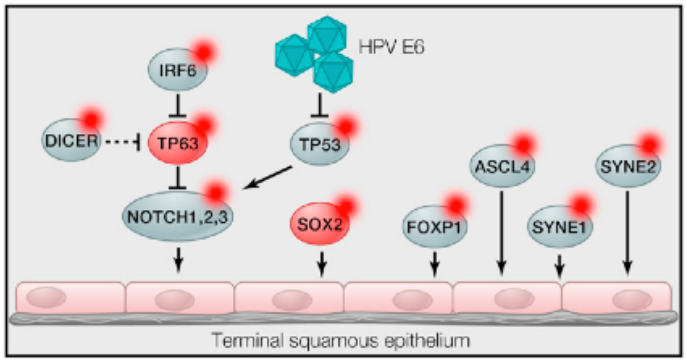
Systematic studies of the cancer genome have exploded in recent years. These studies have revealed scores of new cancer genes, including many in processes not previously known to be causal targets in cancer. The genes affect cell signaling, chromatin, and epigenomic regulation; RNA splicing; protein homeostasis; metabolism; and lineage maturation. Still, cancer genomics is in its infancy. Much work remains to complete the mutational catalog in primary tumors and across the natural history of cancer, to connect recurrent genomic alterations to altered pathways and acquired cellular vulnerabilities, and to use this information to guide the development and application of therapies.

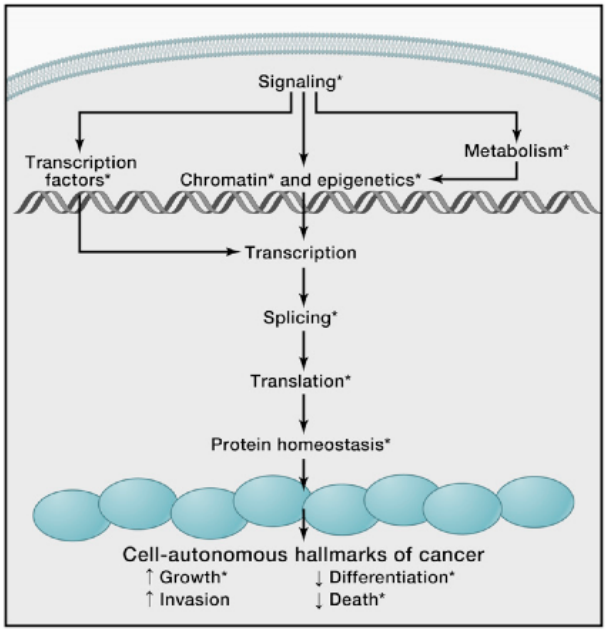
Garraway, *Cell* 153:17, March 2013


Citrate
TCA Cycle
Isocitrate
IDH2
α-KG
α-KG
IDH1/2
2HG
KMT
TET2
KDM
EGLN
+OH
CH3 CH3 CH3
CH3 CH3
CIMP


HDACs
KDMs
KMTs
HATs
TET2
DNMT3A
OH
CH2
CH3
K9 K27
K4 K36
Nucleosome
H3
β-actin
BAF53
ARID1A/B
ARID2
BRG1
SWI/SNF complex
BAF155 BAF170
SNF5
BAF60
BAF45
BAF57
CHD4
CHD1
Compacted chromatin


U1 snRNP
SFRS2
U2 snRNP
SF3B1
ZRSR2
U2AF2
U2AF1
SFRS1
5' exon AG GUAAGU
CURACU Yn AG G 3' exon


HPV E6
IRF6
DICER
TP63
TP53
NOTCH1,2,3
SOX2
FOXP1
ASCL4
SYNE1
SYNE2
Terminal squamous epithelium


Signaling*
Transcription factors*
Chromatin* and epigenetics*
Metabolism*
Transcription
Splicing*
Translation*
Protein homeostasis*
Cell-autonomous hallmarks of cancer
↑ Growth*
↑ Invasion
↓ Differentiation*
↓ Death*

Goals

- To test SBGN representation of real biological pathways in journal.
- To reach out bench biologists and encourage more people to use SBGN.
- To gather feedback to see the area to improve.
- To convince journal to support SBGN.

Current one

Cell

PolyQ Proteins Interfere with Nuclear Degradation of Cytosolic Proteins by Sequestering the Sis1p Chaperone

Sae-Hun Park,[1] Yury Kukushkin,[1] Rajat Gupta,[1] Taotao Chen,[1,2] Ayano Konagai,[1,3] Mark S. Hipp,[1] Manajit Hayer-Hartl,[1] and F. Ulrich Hartl[1,*]

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http://dx.doi.org/10.1016/j.cell.2013.06.003

SUMMARY

Dysfunction of protein quality control contributes to the cellular pathology of polyglutamine (polyQ) expansion diseases and other neurodegenerative disorders associated with aggregate deposition. Here we analyzed how polyQ aggregation interferes with the clearance of misfolded proteins by the degradation by the ubiquitin-proteasome system (UPS) or autophagy (Rubinsztein, 2006). These mechanisms must be tightly regulated to maintain proper proteome balance. Failure of proteostasis control has been associated with the age-dependent manifestation of a number of neurodegenerative aggregate-deposition diseases, including Parkinson's and Huntington's disease. Multiple lines of evidence suggest that ongoing protein aggregation further compromises the proteostasis system, aggravating cellular pathology (Douglas and Dillin, 2010; Gidale-

Park, *Cell*, 154:134, July 2013.

SBGN-PD

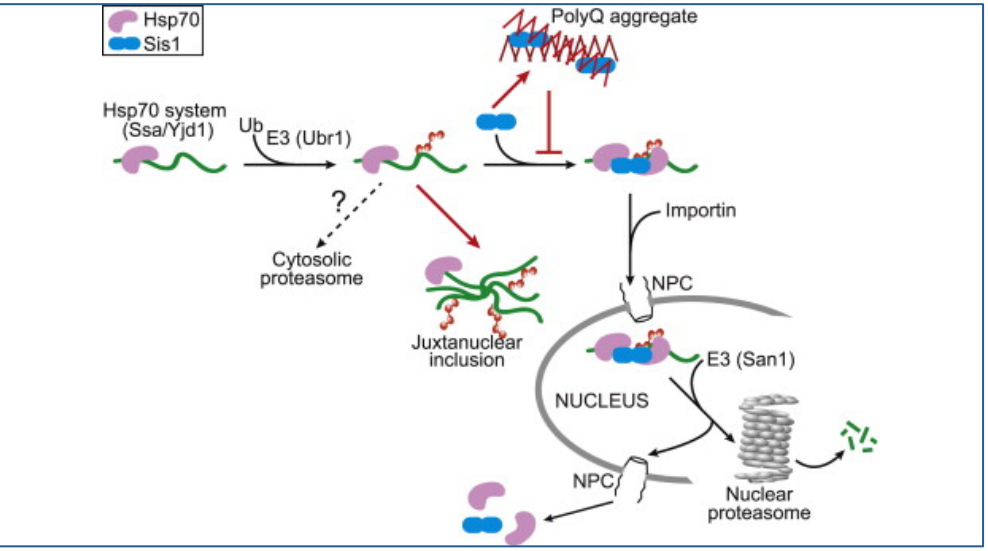
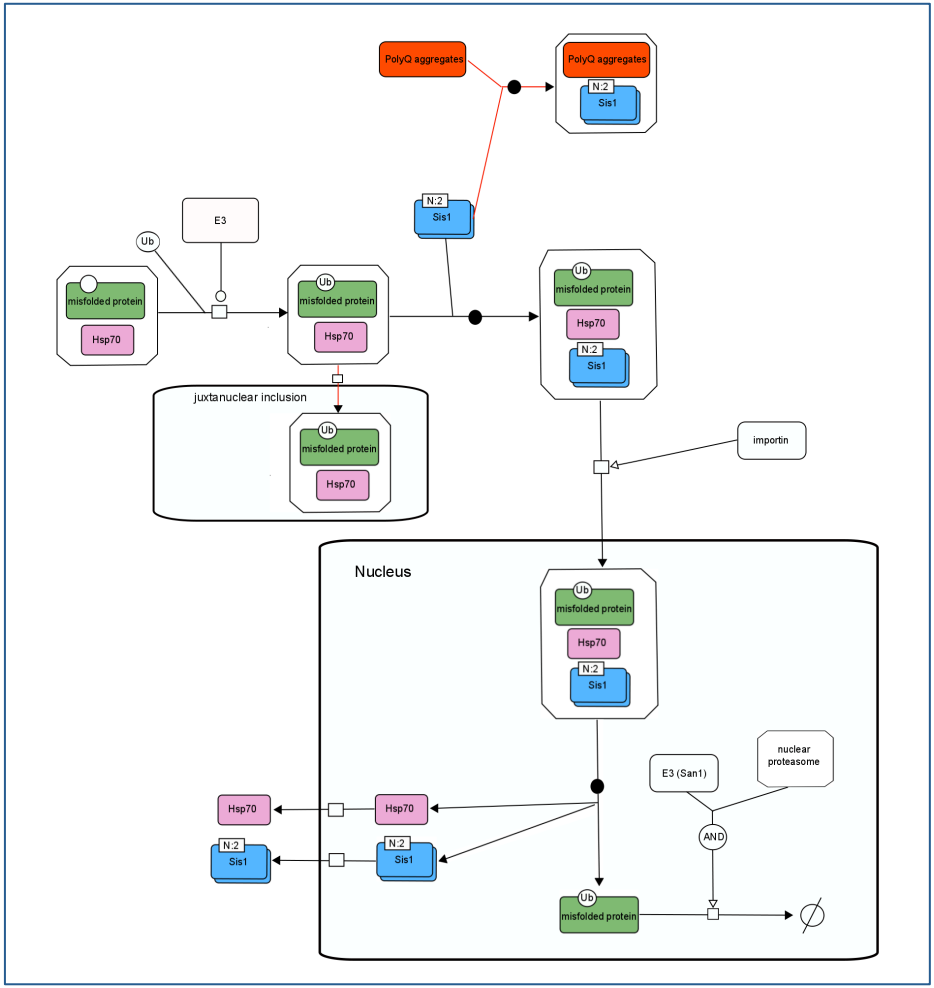


Figure 7, Park et. al, *Cell,* 154:134



Plan

- Publish on the SBGN website.
- Try to publish one each month or every other month.

Questions

- Who will do it?
  - Volunteer sign up
- How to review?
  - SBGN discussion mailing list
  - Should we contact the original author(s)?