# Translation of TCGA data

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# TCGA GBM program: summary

- **Defining the atlas of changes in human GBM**
  - Deeper insights into known mutations
  - Many novel gene candidates identified
  - Cross-platform validation & interpretation of alterations

- **Distinct molecular subtypes of primary GBM defined**
  - Potential implication for patient stratification

- **New technology for sequencing**
  - More data, better data, lower cost…
  - New ways of looking at cancer genomes
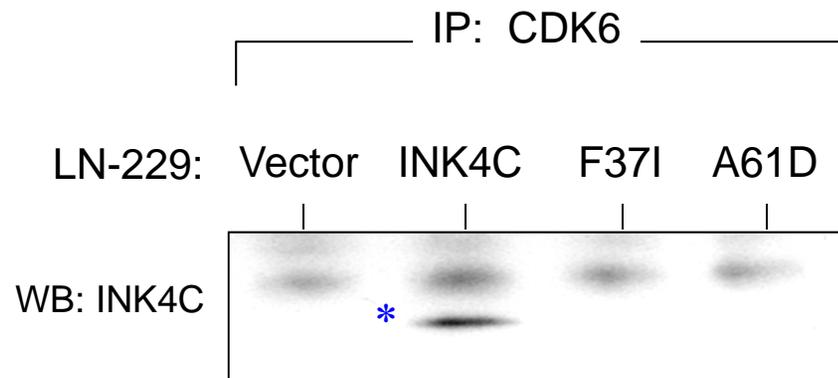
# Integration and Synergy
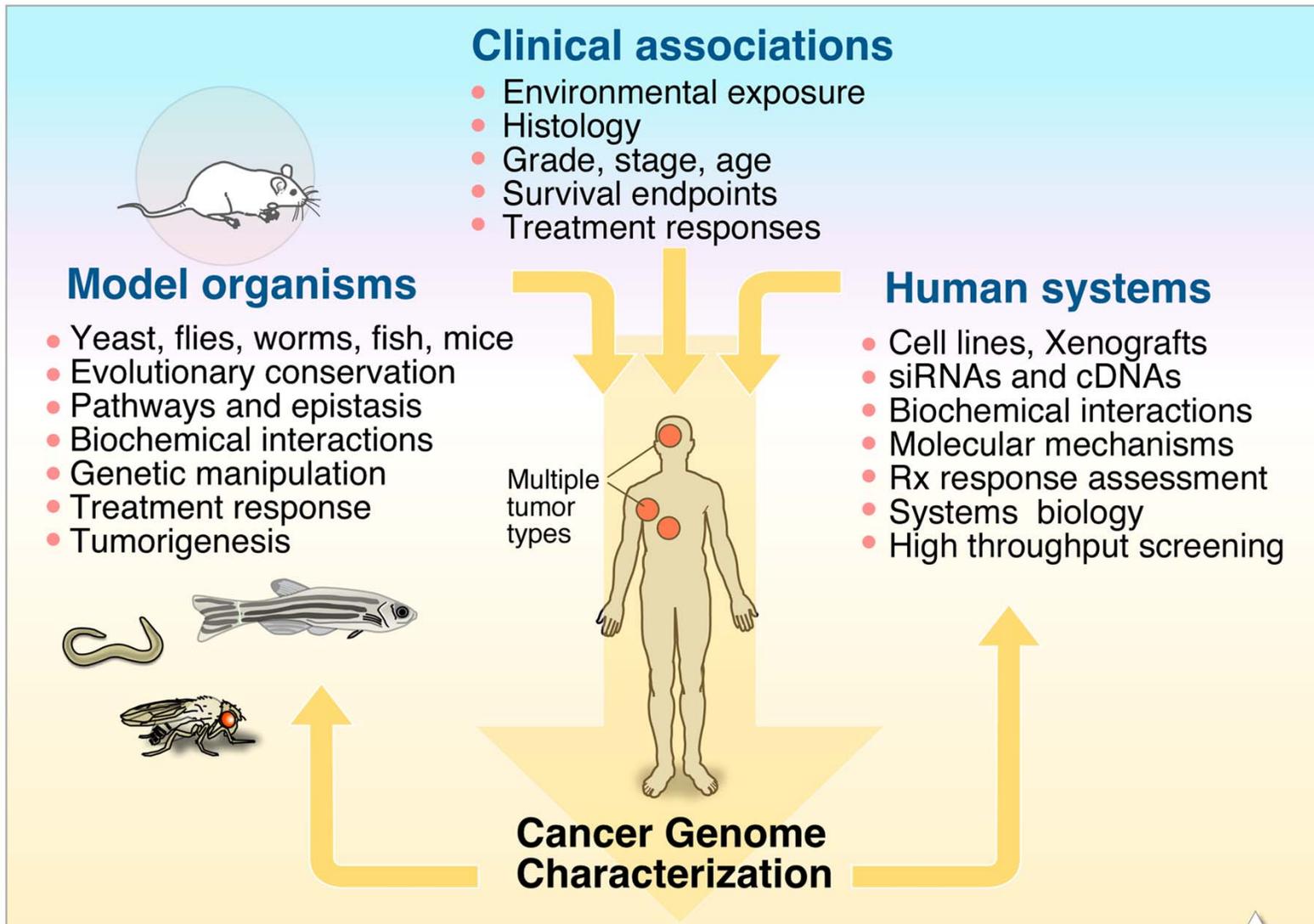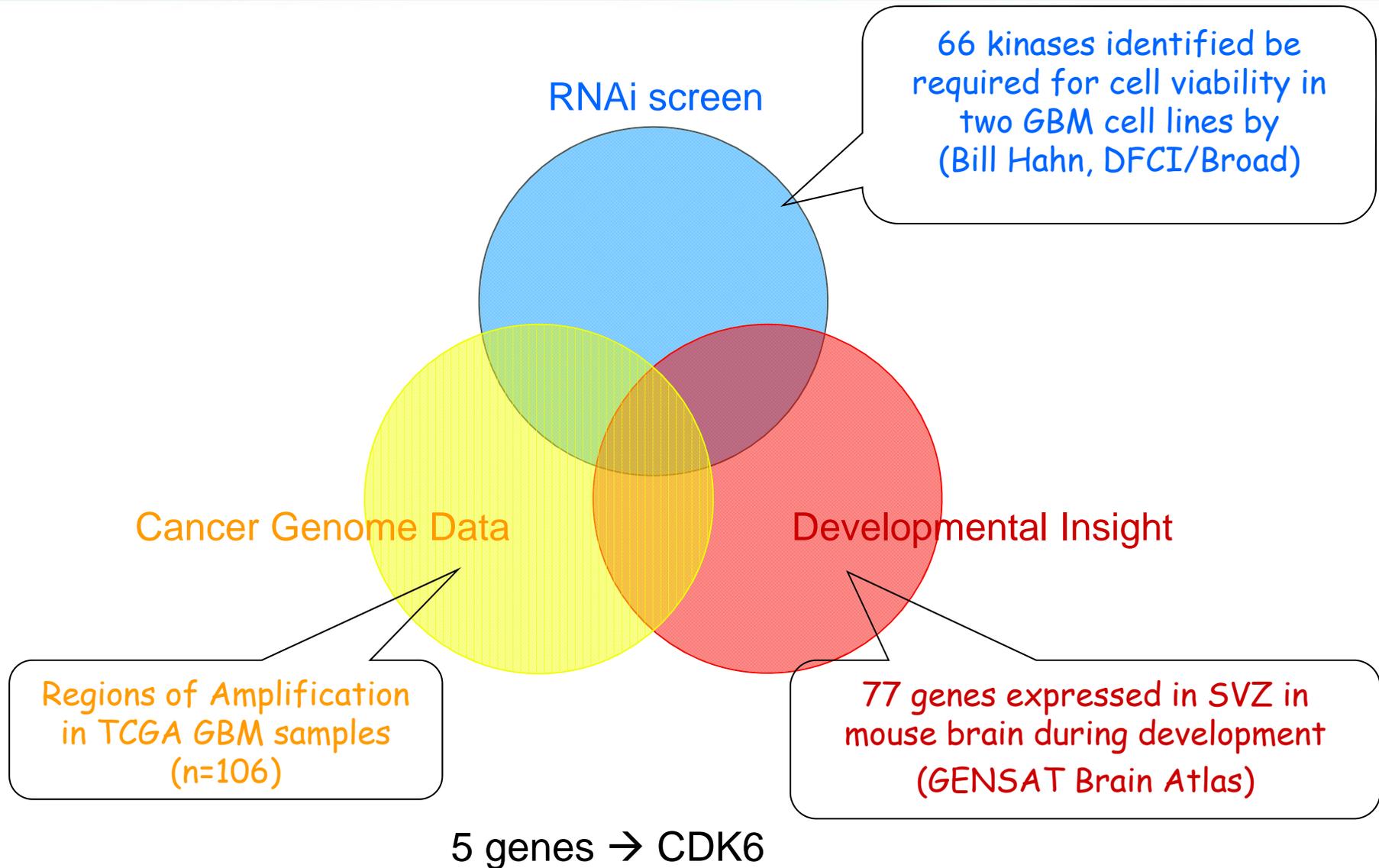
# CDK6 and p18$^{INK4C}$ in GBM

- CDK6, not CDK4, is the major CDK that complexes with p16$^{INK4A}$ or p18$^{INK4C}$ on co-IP
- p18$^{INK4C}$ loss-of-function mutants do not bind to CDK6



- p18$^{INK4C}$ is a backup tumor suppressor engaged in the relatively common setting of p16$^{INK4A}$ inactivation
  - Loss of p16$^{INK4A}$ → enhanced proliferation → increased E2F1
  - E2F1 binding to p18$^{INK4C}$ promoter → induction of backup

Wiedemeyer, Brennan, et al, *Cancer Cell*, in press

# Integration and Triangulation

**Clinical associations**
- Environmental exposure
- Histology
- Grade, stage, age
- Survival endpoints
- Treatment responses

**Model organisms**
- Yeast, flies, worms, fish, mice
- Evolutionary conservation
- Pathways and epistasis
- Biochemical interactions
- Genetic manipulation
- Treatment response
- Tumorigenesis

**Human systems**
- Cell lines, Xenografts
- siRNAs and cDNAs
- Biochemical interactions
- Molecular mechanisms
- Rx response assessment
- Systems biology
- High throughput screening

Multiple tumor types

**Cancer Genome Characterization**