Gene expression

D2.2 · HL only

The same genome can support different cell functions

Explain regulation before attributing a phenotype to a mutation

D2.2 is HL only: expression, regulatory DNA and proteins, message lifetime, epigenetic inheritance, environmental evidence and bacterial control.

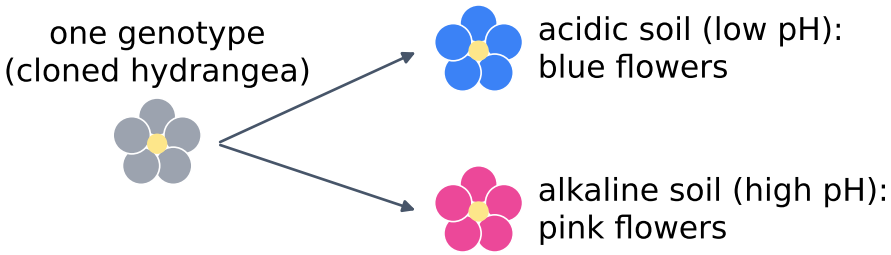
Use transcription and translation from D1.2. A change in expression need not change the DNA base sequence.

Diagrams and calculation datasets are invented teaching models. Named environmental and twin studies are distinguished from them.

Connect an expressed gene with a functional outcome

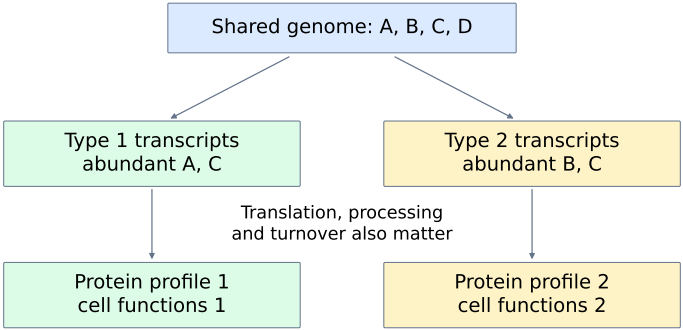
1. **Information.** DNA is transcribed into RNA; a protein-coding message can be translated into a polypeptide.
2. **Function.** Folding and processing can produce an active enzyme that changes a metabolic reaction and phenotype.
3. **Limits.** Some expressed genes produce functional RNA rather than protein. More RNA alone does not establish more active enzyme.

The environment shapes phenotype



Phenotype = genotype + environment

Explain different cell functions without removing unused genes



Invented gene labels; presence is different from abundance and activity

Selective expression changes cell products and function.

A measurement samples one level of expression

Set	What is measured?
Genome	Genetic material; most nucleated body cells share essentially the same genome
Transcriptome	RNA transcripts present in a specified cell, condition and time
Proteome	Proteins present in that context
Inference limit	RNA abundance does not directly establish protein abundance or activity

Differentiation maintains different expression programmes

Separate retained information from current use

Two nucleated cell types can retain genes A–D but produce different combinations of RNA and proteins.

Regulation, RNA lifetime, translation, protein processing and turnover all influence the final products.

Define the tissue, time and treatment when comparing transcriptomes or proteomes. A gene absent from an RNA sample is not necessarily absent from DNA.

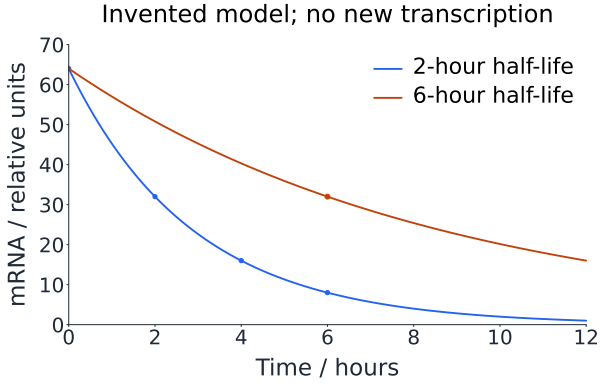
DNA sequences and their binding proteins are different components

Component	Role
Promoter	Regulatory DNA involved in assembling transcription machinery
Enhancer	Regulatory DNA that can influence transcription from a distance
Transcription factor	Protein that binds regulatory DNA and/or participates in regulatory complexes
DNA folding	Can bring distant regulatory regions and associated proteins into proximity
Outcome	Depends on the complex and chromatin context; binding is not universally activating

A steroid hormone can change expression in a responsive cell

1. **Signal.** Cortisol enters a cell with an appropriate intracellular glucocorticoid receptor.
2. **Regulation.** Activated receptor works with regulatory DNA and other proteins to alter transcription of particular targets.
3. **Distinction.** The hormone is not a promoter or a DNA base change. A transcriptional response differs from immediately activating an existing enzyme.

Compare message persistence when new transcription stops



Slower degradation preserves more of the original message.

Follow repeated halving instead of subtracting a fixed amount

1. **Invented model.** 64 relative units initially; half-life two hours; no new transcription.
2. **At two, four and six hours.** 32, 16 and 8 units remain. A six-hour half-life instead leaves 32 units at six hours.
3. **Limit.** Nucleases degrade RNA. Actual lifetimes range from minutes to days; the model does not specify protein lifetime or activity.

An abundant message can have more than one explanation

Separate production from loss

Observed RNA abundance depends on transcription and degradation. Higher RNA can reflect faster production, slower loss or both.

Longer persistence can allow more translation opportunities, but translation efficiency and protein turnover still matter.

A decay comparison needs controlled sampling, a stated initial amount and a justified treatment of continued transcription.

Specify the location and context of an epigenetic change

Modification	**Interpretation**
Promoter cytosine methylation	Often associated with transcriptional repression
Histone methylation	Can activate or repress, depending on the modified site and context
Base sequence	Adding a methyl tag is different from substituting C with another base
Phenotype	Expression may change while the DNA base order is retained

Avoid treating every methyl group as an off switch

A molecular mark needs a regulatory context

Chromatin packaging and access to regulatory regions influence transcription. Epigenetic marks participate in that regulation.

Methylation of a promoter and methylation of a particular histone residue are different molecular changes.

A measured association between a mark and expression does not alone prove that the mark directly caused the expression change.

Distinguish persistence in a cell lineage from transmission to offspring

1. **Mitotic lineage.** Maintenance or restoration of marks can help daughter cells retain a differentiated expression programme.
2. **Between generations.** Transmission requires relevant information to survive or be re-established through reproductive processes.
3. **Resetting.** Extensive resetting occurs during germ-line and early development; most marks do not simply pass unchanged forever.

Parent-of-origin regulation is a controlled exception

Explain imprinting without claiming that all marks escape resetting

Some parent-of-origin marks are protected or maintained in ways that affect offspring expression.

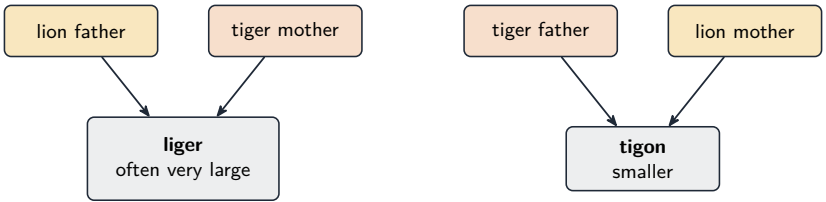
Imprints are also re-established in the germ line according to the sex of the individual producing gametes.

Persistent differentiation in body cells is not itself evidence that an acquired exposure effect will be inherited by grandchildren.

Reciprocal hybrids illustrate a parent-of-origin question

Cross	Interpretation
Male lion × female tiger	Liger
Male tiger × female lion	Tigon
Common growth contrast	Ligers commonly show greater growth than tigons
Teaching model	Parent-of-origin regulation may contribute; species interactions and maternal effects also matter
Evidence limit	Size alone does not establish one specific imprinted gene as the sole explanation

Parent of origin matters



same two species, reversed parent of origin: different growth fits an imprinting model
(parent-specific expression of growth genes)

> Imprinted genes act differently from each parent

Interpret a controlled exposure study at its measured endpoint

1. **Named study.** Cardenas and colleagues (2021): 13 volunteers in a randomized crossover comparison of diesel exhaust and clean air.
2. **Measurement.** Methylation differences at particular sites in sampled bronchial epithelial cells.
3. **Boundary.** This is not a demonstration of all genes changing, inevitable disease, lifetime persistence or inheritance by descendants.

Design controls answer some questions and leave others open

Match the claim to the tissue, measurement and duration

A crossover comparison reduces some differences between participants; sequence, washout and exposure conditions still matter.

Different tissues can show different methylation patterns. Sampling one tissue does not measure every organ.

To argue inherited effects, separate direct exposure of a generation from transmission beyond it and test persistence of the relevant information.

Evaluate a twin study without treating age as randomized

1. **Named study.** Fraga and colleagues (2005): 40 monozygotic twin pairs, ages 3–74, with methylation and histone-acetylation measures.
2. **Count.** 14 of 40 pairs differed in the reported global epigenetic measures: 35% of pairs, not 35% of genes.
3. **Limit.** Age and life-history associations do not isolate one cause; epigenetic drift and tissue sampling also matter.

Use shared ancestry as a comparison, not a claim of identical lives

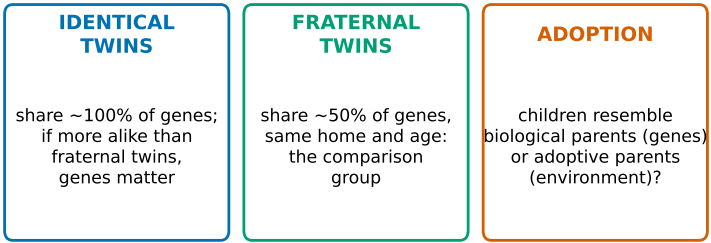
Expression evidence requires its own measurement

Monozygotic twins have very similar inherited DNA, but environments, cell histories and stochastic events can differ.

The study compared expression in selected younger and older pairs; not every expression measurement covered all 40 pairs.

Histone acetylation measured in this study is different from histone methylation. Neither twins nor correlations alone identify a unique causal exposure.

Separating genes and environment

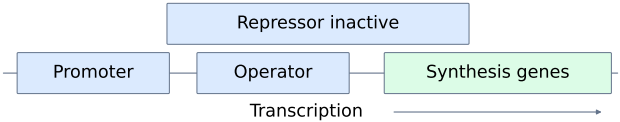


heredity and environment interact: these studies estimate how much each explains, not which one wins

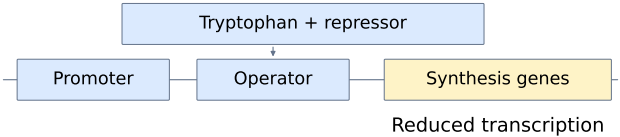
Adopted children compare biological and adoptive parents

Use tryptophan availability to explain transcriptional feedback

Low tryptophan



High tryptophan



Repression model only; DNA sequences and protein are different components

End-product binding changes repressor activity.

Low tryptophan permits synthesis-gene transcription in this model

1. **Regulatory protein.** Without sufficient tryptophan, the repressor is ineffective at blocking the operator.
2. **DNA and RNA.** Transcription of the biosynthetic genes can proceed from the promoter.
3. **Consequence.** Expression supports synthesis of a scarce end product. This is a repression model, not every layer of real operon control.

High tryptophan reduces transcription through a corepressor

1. **Molecular interaction.** Tryptophan binds the repressor, increasing its effective operator binding.
2. **DNA binding.** The active complex binds the operator and reduces transcription of the synthesis genes.
3. **Do not conflate.** Tryptophan is a small molecule; repressor is protein; promoter/operator are DNA. This differs from directly inhibiting an existing enzyme.

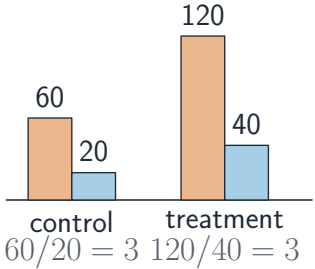
A level ratio and a percentage increase answer different questions

1. **Invented comparison.** Control 3 units; treatment 12 units with comparable measurement.
2. **Fold level.** $12/3 = 4$ times the control level.
3. **Increase.** $(12 - 3)/3 \times 100 = 300\%$. Fourfold level is not a 400% increase.

Normalize before interpreting an apparent rise

1. **Invented counts.** Control target/reference = 60/20; treatment = 120/40.
2. **Normalized comparison.** Both ratios equal 3; treatment/control normalized fold change = 1.
3. **Inference.** Raw target counts doubled, but reference counts also doubled. Check reference stability, sampling, replication and protein evidence.

Normalise before you compare



target signal
reference signal

normalised fold change $= 3/3 = 1$

despite twice the raw target signal

and 12 vs 3: fold change 4,

an increase of 300%, not 4%

Fold change $= 3 \div 3 = 1$: no change

Attempt the thirteen handout questions

Separate the mechanism, the calculation and the strength of evidence

Explain genome/transcriptome/proteome, regulatory DNA/proteins, cortisol and message decay.

Evaluate epigenetic inheritance, reciprocal hybrids, environmental exposure and twin evidence; explain trp repression.

Calculate level ratio, percentage increase and normalized expression. Give a limit to each interpretation.

Check the independent numerical answers

1. **Decay and twin sample.** 80 units with a 10-minute half-life leaves 10 after 30 minutes. $14/40 \times 100 = 35\%$ of pairs.
2. **Expression.** $20/4 = 5$-fold level; $(20 - 4)/4 \times 100 = 400\%$ increase.
3. **Normalization.** $45/15 = 3$ and $90/30 = 3$. Normalized fold change $= 1$, despite a twofold raw target count.

Check yourself

Use the exact molecule, denominator and inheritance route

Promoter/enhancer/operator are DNA; transcription factors and repressors are proteins. Hormone signals need responsive machinery.

RNA abundance is not automatically active protein. Fold level, percentage increase and normalized fold change need separate calculations.

Promoter and histone methylation are not interchangeable rules. Cell-lineage persistence, direct exposure and inheritance across generations are different claims.