### RNAP III Termination

RNAP III transcribes several non-coding RNAs including transfer RNA, 5S rRNA, U6 snRNA, adenovirus-associated (VA) RNA, and 7SK RNA (▶ Transcription in Eukaryote). RNAP III transcription terminates efficiently by the simple T-rich element without other termination factors' involvement, indicating that RNAP III itself has the termination ability. In mammals, four Ts is found commonly as terminator sequence located within 40 bp downstream from the mature 3′ end of the RNAP III–transcribed RNAs. On the other hand, the most frequent T length in yeast is six or seven. The downstream sequence from T-track appears to have the effect for the pausing time which provides the processing time (Braglia et al. 2005). However, RNAP III termination mechanism is still obscure, and necessitates further study, especially for the accessory factors.

## Cross-References

- ▶ Heterochromatin and Euchromatin
- ▶ Histone Post-translational Modification to Nucleosome Structural Change
- ▶ Nucleosome Structure
- ▶ Transcription Elongation, Mechanisms
- ▶ Transcription in Eukaryote
- ▶ Transcription Initiation in Eukaryote

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# Mechanism, Conserved

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## Definition

A biological ▶ mechanism is conserved when it can be identified as the product of evolutionary descent. Considerations of conservation are important in determining whether findings about a mechanism in a ▶ model organism can be generalized to target organisms. If the mechanisms are conserved, then researchers expect the similarities between model and target to be deep so that discoveries about the model support inferences about the target. Conservation is ultimately established through phylogenetic analyses and is explained through processes of development and evolution.

## Characteristics

### The Role of Conservation in Generalizing Research on Biological Mechanisms

Much of modern biology has focused on the discovery of mechanisms. Recent philosophical analysis has characterized mechanisms as consisting of parts (or entities) performing operations (or activities) organized (see ▶ Organization) to produce a phenomenon (Bechtel and Abrahamsen 2005; Machamer et al. 2000). In response to developments, such as systems biology, some philosophers have begun to couple accounts of mechanism to dynamical models, yielding dynamic mechanistic explanations (see ▶ Mechanism, Dynamic). Mechanistic research is typically conducted on specific model organisms (gene expression in

*Neurospora* or circadian rhythms in *Drosophila*). This presents the challenge of how findings from such research are to be generalized to target organisms (often humans). A common strategy is to appeal to the conserved nature of biological mechanisms where conservation is due to evolution, a process of descent with modification.

Both evolutionary descent and modification are important to the practice of generalization in mechanistic research. When organisms possessing a particular mechanism are linked by evolutionary descent (even when they fall within separate branches of a phylogenetic tree), researchers assume deep commonalities between the mechanisms such that when a part or operation is found within a model mechanism, they expect to find it and search for it within the target mechanism. However, researchers are not surprised to discover differences between model and target due to evolutionary modification and recognize the need to adjust their account of the mechanism appropriately. For example, model systems are often chosen for their relative simplicity. Research on the model can then be highly informative about the basic way in which the mechanism produces the phenomenon. Yet, the target may well involve additional parts and operations such as increased regulatory components that modulate the working of the mechanism. Moreover, the increase in parts may stem from gene duplication, with each daughter gene or protein specializing in a somewhat different operation. Far from simply refuting the relevance of the model, the discovery of such modifications spurs further research that is still guided by the model, as will be illustrated below.

The importance of descent can be seen by recognizing that similar mechanisms can also arise through ► convergent evolution. In this process, selection favors an ► adaptation in each lineage to produce mechanisms generating very similar phenomena. When two mechanisms are the product of convergent evolution, there is little reason to expect deep similarities. This is because mechanisms with distinct evolutionary histories will often bring different entities, activities, and organizational structures to bear on the same adaptive problem.

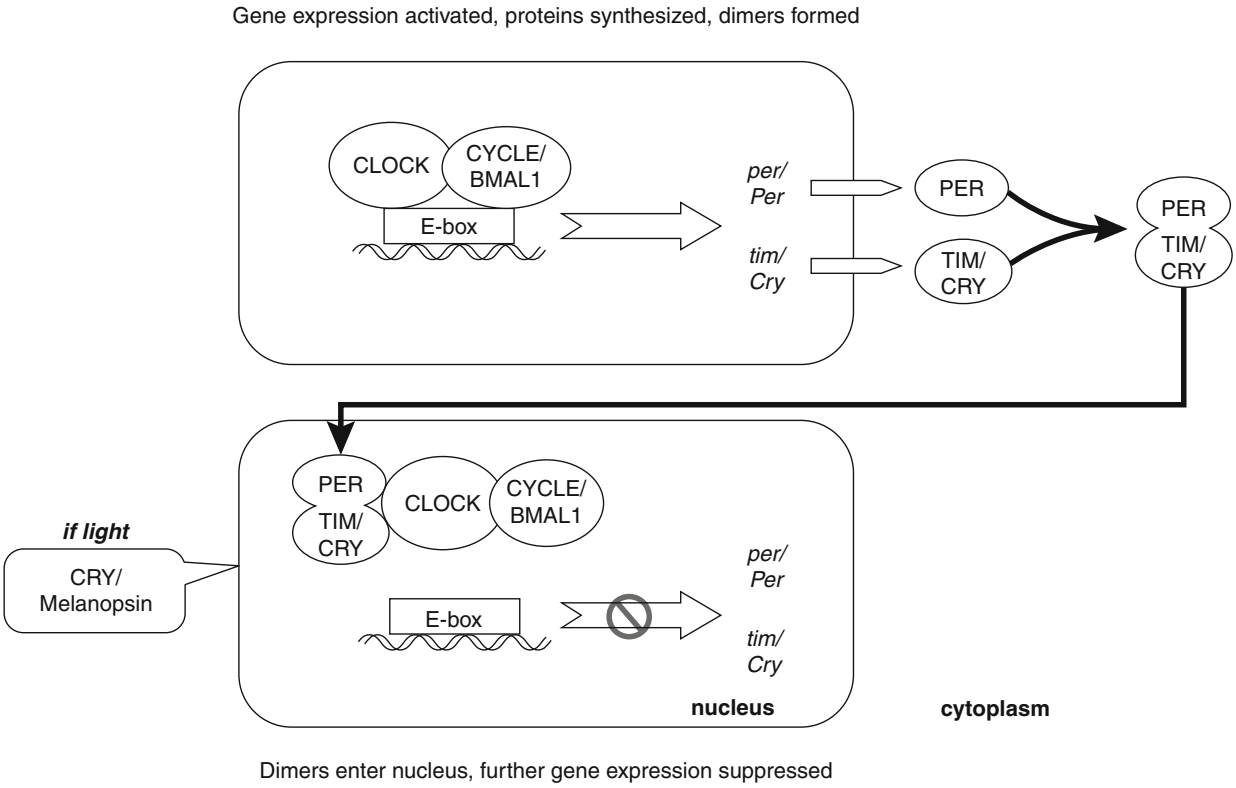
## Identifying and Explaining Conserved Traits

Establishing homology is crucial to determining whether mechanisms are conserved. The notion of homology predates the acceptance of evolution. Richard Owen, for example, defined a homolog as "the same organ in different animals under every variety of form and function," using qualitative characteristics to determine sameness (Owen 1843). With the acceptance of evolution, descent became a necessary criterion for sameness. However, qualitative criteria, such as relative position and the presence of complex and unique properties (Remane 1952), are still important for identifying potential homologs. Molecular biologists employ the term *homology* for descent relations in addition to those of evolutionary descent, most notably for traits arising from gene duplication (paralogues) and from horizontal gene transfer (xenologues). In establishing the conservation of mechanisms, one must appeal to what is sometimes called the taxic or phylogenetic approach to homology, which includes only those traits that are similar because they derive from a common ancestor.

Determining whether a trait is conserved requires establishing the phylogenetic relationships of the organisms exhibiting that trait. If the most parsimonious explanation (one making the fewest assumptions) for the presence of a trait within a monophyletic group is inheritance from a common ancestor, then that trait is regarded as conserved across those individuals that possess it (Hall 1994). However, identifying a conserved trait does not provide an explanation of how it has remained relatively invariant over evolutionary time. That requires consideration of the developmental and evolutionary processes involved in the perpetuation and maintenance of traits across generations, a key area of research in the field of evolutionary developmental biology (see ► Explanation, Developmental; and ► Explanation, Evolutionary).

## Conserved Mechanisms

In applying the conservation of traits to mechanisms, one can focus on the parts of a mechanism (genes, proteins, cell types, or morphological structures) or the operations performed by the parts (catalyzing a reaction, capturing free energy, generating action potentials). Often these go together. Accordingly, researchers provisionally assume that if a gene is conserved, it performs that same function in the target organism. Likewise, they assume that if a function is conserved, so is the responsible part. However, parts and operations can be dissociated so that a part of a mechanism is conserved, while its operation changes over evolutionary time, and vice versa. Even in such




**Mechanism, Conserved, Fig. 1** A comparison of part of the circadian mechanism in insects and mammals. Where two names are shown, the *top* is the gene or protein in the insect mechanism and the *bottom* is the gene or protein in the mammalian mechanism

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cases, though, conservation plays an important heuristic role: discovery that a part is not performing the operation in the target organism prompts research directed at finding other parts that could perform the conserved function.

These uses of conservation in research can be illustrated by examining the circadian mechanism in insects and mammals (see Bechtel 2009; for additional examples, Hall 1994). The mechanism in both classes is organized in the same way, employing a transcriptional feedback loop with negative and positive loops (see ► Gene Regulation). The negative feedback loop in insects involves the gene *period* (*per*), which is transcribed, transported into the cytoplasm, and translated into the protein PER. Over time PER is transported back into the nucleus where it inhibits the transcription of its own gene until it degrades, resulting in regular oscillations of PER concentrations – a crucial component of the circadian clock. The assumption that this mechanism was conserved across insects and mammals guided researchers to search for homologs of *per* in mammals, where they found three, two of which were found to perform the same basic operation.

However, not all homologs in the circadian mechanism perform the same operation in insects and mammals (Fig. 1 compares one part of the mechanisms in these two classess). In insects, PER dimerizes with a second protein, TIMELESS (TIM), before entering the nucleus. TIM also has a homolog in mammals, but it was discovered not to perform the same operation. The resulting search for another protein that performs this operation in mammals led to finding a cryptochrome (CRY). Thus, different proteins (CRY in mammals and TIM in insects) were found to perform the same activity (dimerizing with PER) within the circadian mechanism. Moreover, insects also contain a CRY protein. Researchers initially assumed that this protein was a homolog of mammalian CRY, but later determined that it was not. Nevertheless, insect CRY was found to play an important role in regulating circadian oscillations; it initiates the breakdown of TIM upon exposure to light, thereby entraining oscillations to the external day/night cycle.

When mammalian CRY was not found to perform this operation, researchers again searched for another compound (melanopsin) that did.

Across the different orders of life in which circadian rhythms are studied (cyanobacteria, fungi, plants, and animals) most parts and operations are not conserved, leading many researchers to assume that the mechanisms are convergent. However, in all but cyanobacteria the organization of the mechanism is extremely similar prompting a few researchers to explore the possibility that organization might be conserved while different parts came to perform the specific operations in them. This hypothesis, supported by the determination that some of the ancillary components of the mechanism (e.g., various kinases) appear to be homologous, supports generalizing results about overall organization of the mechanism across the orders of life.

A mechanism may be more likely to be conserved if it functions as a module. A process is modular when it is internally integrated and relatively autonomous from and so unaffected by changes to other parts of the organism. The autonomous nature of modules also suggests that they can be embedded as units into new contexts. Examples of mechanisms that have been identified as modules include gene networks, signaling pathways, cell types, and organs (Schlosser and Wagner 2004).

Though traits and mechanisms can be conserved across species, it is important to keep in mind that conservation does not occur in isolation. A biological system can be conserved in part, while also being affected by adaptive pressures, mutations, duplication events, and the recruitment of other molecular elements. Given this, when evaluating the potential conservation of a mechanism, the biological, developmental, and environmental constraints affecting a species over evolutionary time must be taken into account on a case-by-case basis.

## Cross-References

- ▶ Adaptation
- ▶ Convergent Evolution
- ▶ Explanation, Developmental
- ▶ Explanation, Evolutionary
- ▶ Gene Regulation
- ▶ Mechanism
- ▶ Mechanism, Dynamic
- ▶ Model Organism
- ▶ Organization

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# Mechanism, Dynamic

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## Synonyms

Computational models of mechanisms; Dynamic mechanistic explanation

## Definition

Biological mechanisms continually change their behavior over time. Understanding such change presents a challenge for traditional mechanistic research, which emphasizes decomposing mechanisms to identify their relatively stable parts and operations. Understanding patterns of change in mechanisms requires