striped moving pattern, then when the motion is stopped the stripes appear to move back in the opposite direction. This motion aftereffect can be built up to one eye and elicited from the other eye. Murakami aimed an annular stimulus containing drifting stripes at the blind spot of the right eye. Filling-in made this look like a complete striped disk. He then tested with a small striped disk, smaller than the hole in the annulus, and viewed by the corresponding intact retina of the *left* eye. Observers reported a motion aftereffect. This suggests that the motion was actively filled into the blind spot of the right eye.

Further support comes from filling-in of a large disk. A large white disk was flashed up on a black surround, followed 50–100 milliseconds later by a white outline circle of about half the diameter. Observers reported that the interior of the outline circle looked black. If the circle was smaller, the optimal time gap was longer. This suggests that a brightness signal propagates inward from the circumference at an estimated speed of 110–150° of visual angle per second, and is arrested by the barrier of the outline circle. This is supported by experiments on simultaneous contrast. A static grey disk appears to brighten and dim when its surround respectively dims and brightens, but this process breaks down at repetition rates exceeding 2.5 Hz, suggesting also a spreading process at a finite speed. Similar effects have been shown for the filling-in of texture.

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Tudor domain

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What is the Tudor domain? The Tudor domain was first identified as a segment of approximately 60 amino acids that is present in 11 repeated units in the *Drosophila* protein of the same name. *Drosophila tudor* was first identified genetically, in a large-scale screen for maternal-effect lethal mutations that affected embryonic development. Several complementation groups of such mutations were identified in which homozygous females produced embryos that failed to specify primordial germ cells, and these were named after extinct European royal families (*tudor*, *vasa*, *valois*, and *staufen*). Since that time, over 200 Tudor-domain containing proteins have been identified from essentially all varieties of eukaryotes, including plants, animals, and fungi, but not from prokaryotes. Tudor domains are related to Chromo, MBT, PWWP, and Agenet-like domains, which are implicated in chromatin binding. The core Tudor domain forms a β-barrel like core structure that contains four short β-strands followed by an α-helical region (Figure 1). In different types of Tudor-domain containing proteins, the core Tudor domain or domains can be flanked on the amino-terminal side with other conserved motifs.

What is the function of the Tudor domain? Four types of Tudor domains can be distinguished based on their flanking sequences. The original germ-line type Tudor domain binds to proteins with dimethylated arginine or lysine residues. Work in mammals and *Drosophila* is consistent with a model that arginine methylation of Piwi-type proteins, and their consequent binding to Tudor proteins, is necessary to

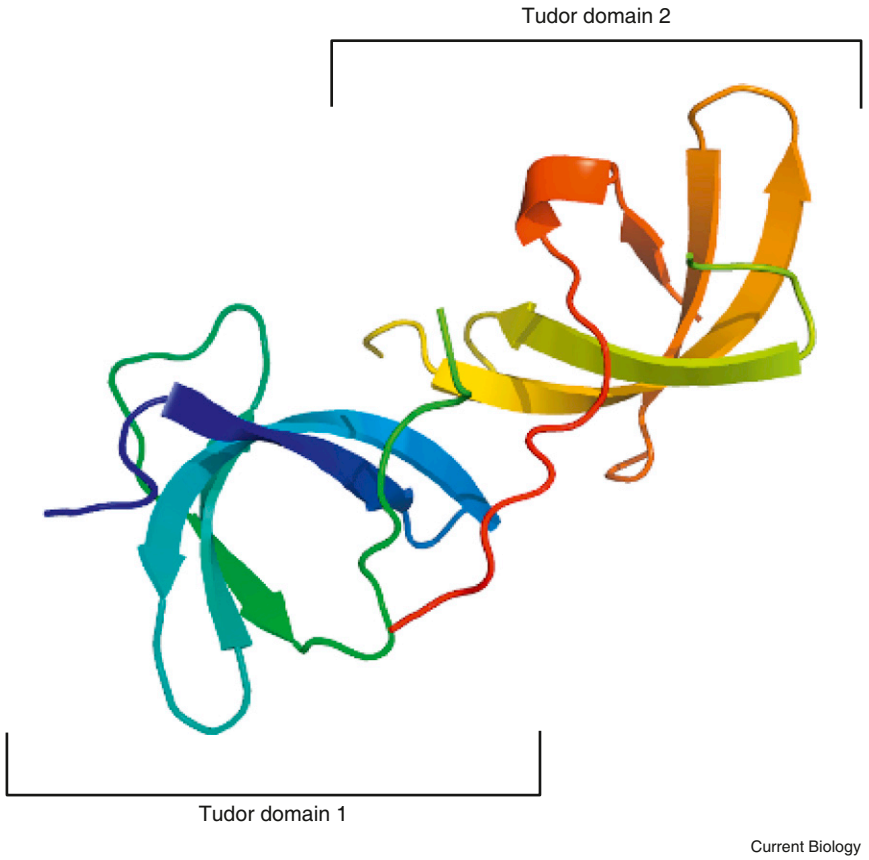

Figure 1. The Tudor domain.

Schematic representation of the structure of the two Tudor domains of the human fragile X mental retardation protein FXR2 (PDB: 3H8Z). The structure was generated by the Structural Genomics Consortium (www.thesgc.org) and placed in the public domain. Each Tudor domain contains four β-strands (depicted by broad colored arrows) that form a barrel structure.

direct the former to a structure called the nuage, which in turn is essential for piwi-interacting RNAs (piRNAs) to silence retrotransposons in germ line cells (Figure 2). Another type of Tudor domain binds methylated histone tails, suggesting that they have a common, perhaps even universal, function of facilitating protein–protein interactions through their ability to bind methylated lysine or arginine. Thus, the Tudor domain operates as a recruitment domain in a manner analogous to the SH2 domain; however, it recognizes methylated amino acids rather than phosphotyrosine.

What kinds of proteins possess Tudor domains? Tudor-domain containing proteins have been linked to chromatin regulation, pre-mRNA processing, spliceosome assembly, the RISC complex (involved in RNA interference), and to germ line development through their involvement in piRNA-mediated transposon silencing. Consistent with those functions, Tudor domains can be found together in the same polypeptide as various RNA-binding motifs (DEAD-box or KH-domain), chromatin-binding domains (Chromo, PHD finger), DNA-binding domains (BRIGHT), and several others. Most processes in which Tudor-domain containing proteins have been implicated involve the activity of large, supramolecular complexes, which may indicate a key role for the Tudor domain in their assembly or in regulating their stability.

What role do Tudor-domain containing proteins have in germ cell specification? Embryos produced by *tudor* mutant females usually lack several posterior segments, although even from *tudor*-null females a small proportion of embryos are correctly patterned and viable. The effects of *tudor* mutations on germ cell specification are more severe; embryos produced from females carrying most *tudor* alleles do not specify primordial germ cells and therefore completely lack a germ line. In flies there is no known role for *tudor* in male germ line development; conversely its mouse counterparts TDRD1, 2, 4, 6, 7, 8, and 9 are linked to male, and not female, germ line development. This is also true for *vasa*, suggesting that a primordial female-specific genetic pathway

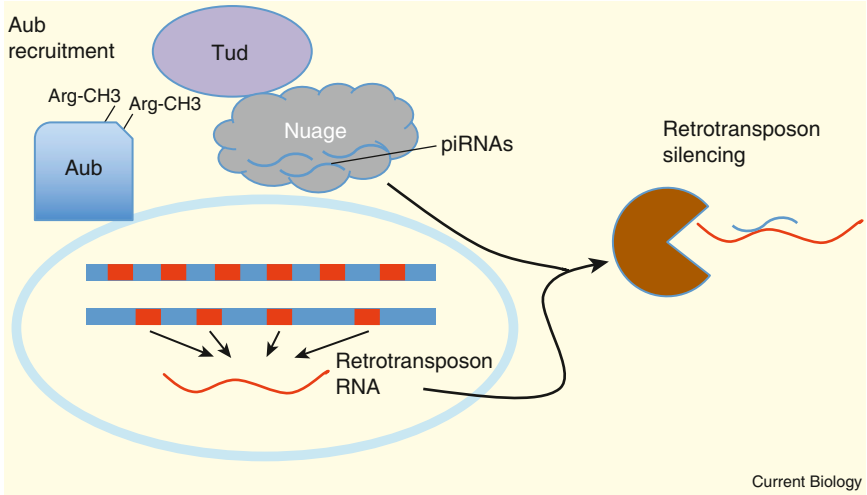

Figure 2. Tudor is linked to retrotransposon silencing in germ line cells.

In mammals and *Drosophila*, Tudor has a critical role in retrotransposon silencing. Symmetric dimethylation of arginine residues of Aub is essential for recruitment of Tudor (Tud), which binds these residues through its Tudor domains. The association of Tud with Aub is essential for recruitment of Aub to the nuage, germ line specific ribonucleoprotein particles that are located near the outer surface of the nuclei. The nuage also contains piRNAs, which are involved in silencing retrotransposons. For simplicity the figure uses the *Drosophila* nomenclature; mouse counterparts for Aub are MILI, MIWI, and MIWI2; for Tud, TDRD1, 2, 4, 6, 7, 8, and 9. In *Drosophila*, Argonaute3 can function similarly to Aub in germ line cells, while Piwi has a similar function in the soma of the ovary.

involved in germ cell development has persisted in vertebrate males, but has been lost in vertebrate oogenesis. In both mice and flies, Tudor protein accumulates in germ line specific ribonucleoprotein (RNP) complexes called nuage, polar granules, or germinal granules, and this accumulation requires the activity of Vasa, a DEAD-box helicase that may be involved in RNP remodeling. Association of Tudor in the nuage in turn is essential for recruiting Aubergine (Figure 2), which functions in retrotransposon silencing.

Is this the whole story, or does Tudor function in processes other than retrotransposon silencing? The only specific role for Tudor that has been identified thus far is its function in retrotransposon silencing described above. However, it is probable that Tudor has additional functions in germ cell development. Loss of Tudor function alters the population of transposon-derived piRNAs but does not eliminate or grossly derepress any particular class; thus, it is difficult to conclude that germ cells lacking Tudor fail to form because of uncontrolled retrotransposon activity. Tudor may have a role in assembling or stabilizing polar granules, RNP complexes related to nuage that are specifically implicated in germ cell specification, as these structures are far fewer in number and much less electron-dense in *tudor* mutant oocytes.

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