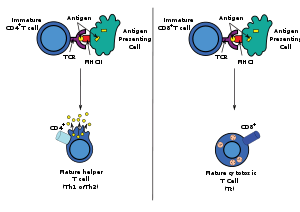
**T-cell receptor**

From Wikipedia, the free encyclopedia

|  |  |
| --- | --- |
| [TCRComplex.png](http://en.wikipedia.org/wiki/File:TCRComplex.png)  The **T-cell receptor complex** with TCR-α and TCR-β chains,[CD3](http://en.wikipedia.org/wiki/CD3_receptor) and ζ-chain accessory molecules. | |
| **Identifiers** | |
| [**Pfam**](http://en.wikipedia.org/wiki/Pfam) | [PF11628](http://pfam.xfam.org/family?acc=PF11628) |
| [**InterPro**](http://en.wikipedia.org/wiki/InterPro) | [IPR021663](http://www.ebi.ac.uk/interpro/entry/IPR021663) |
| [**OPM superfamily**](http://en.wikipedia.org/wiki/Orientations_of_Proteins_in_Membranes_database) | [261](http://opm.phar.umich.edu/families.php?superfamily=261) |
| [**OPM protein**](http://en.wikipedia.org/wiki/Orientations_of_Proteins_in_Membranes_database) | [2hac](http://opm.phar.umich.edu/protein.php?search=2hac) |
| |  |  | | --- | --- | | **Available protein structures:** | | | [**Pfam**](http://en.wikipedia.org/wiki/Pfam) | [structures](http://pfam.sanger.ac.uk/family/PF11628?tab=pdbBlock) | | [**PDB**](http://en.wikipedia.org/wiki/Protein_Data_Bank) | [RCSB PDB](http://www.rcsb.org/pdb/search/smartSubquery.do?smartSearchSubtype=PfamIdQuery&pfamID=PF11628);[PDBe](http://www.ebi.ac.uk/pdbe-srv/PDBeXplore/pfam/?pfam=PF11628); [PDBj](http://pdbj.org/searchFor?query=PF11628) | | [**PDBsum**](http://en.wikipedia.org/wiki/PDBsum) | [structure summary](http://www.ebi.ac.uk/thornton-srv/databases/cgi-bin/pdbsum/GetPfamStr.pl?pfam_id=PF11628) | | |

[](http://en.wikipedia.org/wiki/File:Antigen_presentation.svg)

Antigen presentation stimulates T cells to become either "cytotoxic" CD8+ cells or "helper" CD4+ cells.

|  |  |
| --- | --- |
| **T cell receptor alpha locus** | |
| **Identifiers** | |
| **Symbol** | TRA@ |
| **Alt. symbols** | TCRA |
| [**Entrez**](http://en.wikipedia.org/wiki/Entrez) | [6955](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=retrieve&dopt=default&list_uids=6955&rn=1) |
| [**HUGO**](http://en.wikipedia.org/wiki/Human_Genome_Organisation) | [12027](http://www.genenames.org/data/hgnc_data.php?hgnc_id=12027) |
| [**OMIM**](http://en.wikipedia.org/wiki/OMIM) | [186880](http://www.omim.org/186880) |
| **Other data** | |
| [**Locus**](http://en.wikipedia.org/wiki/Locus_(genetics)) | [Chr. 14](http://en.wikipedia.org/wiki/Chromosome_14_(human)) [*q11.2*](http://omim.org/search?index=geneMap&search=14q11.2) |

|  |  |
| --- | --- |
| **T cell receptor beta locus** | |
| **Identifiers** | |
| **Symbol** | TRB@ |
| **Alt. symbols** | TCRB |
| [**Entrez**](http://en.wikipedia.org/wiki/Entrez) | [6957](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=retrieve&dopt=default&list_uids=6957&rn=1) |
| [**HUGO**](http://en.wikipedia.org/wiki/Human_Genome_Organisation) | [12155](http://www.genenames.org/data/hgnc_data.php?hgnc_id=12155) |
| [**OMIM**](http://en.wikipedia.org/wiki/OMIM) | [186930](http://www.omim.org/186930) |
| **Other data** | |
| [**Locus**](http://en.wikipedia.org/wiki/Locus_(genetics)) | [Chr. 7](http://en.wikipedia.org/wiki/Chromosome_7_(human)) [*q34*](http://omim.org/search?index=geneMap&search=7q34) |

The **T cell receptor** or **TCR** is a molecule found on the surface of [T lymphocytes](http://en.wikipedia.org/wiki/T_lymphocytes) (or T cells)[[1]](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#cite_note-KindtGoldsby2007-1) that is responsible for recognizing [antigens](http://en.wikipedia.org/wiki/Antigen) bound to [major histocompatibility complex](http://en.wikipedia.org/wiki/Major_histocompatibility_complex) (MHC) molecules. The binding between TCR and antigen is of relatively low [affinity](http://en.wikipedia.org/wiki/Affinity_(pharmacology)#Protein-ligand_binding) and is [degenerate](http://en.wikipedia.org/wiki/Degeneracy_(biology)): that is, many TCR recognize the same antigen and many antigens are recognized by the same TCR.

The TCR is composed of two different protein chains (that is, it is a [hetero](http://en.wikipedia.org/wiki/Heteromer)[dimer](http://en.wikipedia.org/wiki/Protein_dimer)). In 95% of T cells, this consists of an alpha (α) and beta (β) chain, whereas in 5% of T cells this consists of [gamma and delta](http://en.wikipedia.org/wiki/Gamma/delta_T_cells) (γ/δ) chains. This ratio changes during ontogeny and in diseased states.

When the TCR engages with antigenic peptide and MHC (peptide/MHC), the T lymphocyte is activated through a series of biochemical events mediated by associated enzymes, co-receptors, specialized adaptor molecules, and activated or released transcription factors.

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* [1 Structural characteristics of the TCR](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#Structural_characteristics_of_the_TCR)
* [2 Generation of the TCR diversity](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#Generation_of_the_TCR_diversity)
* [3 The TCR complex](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#The_TCR_complex)
* [4 TCR co-receptors](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#TCR_co-receptors)
* [5 Associated molecules of the TCR complex involved in T-cell activation](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#Associated_molecules_of_the_TCR_complex_involved_in_T-cell_activation)
* [6 References](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#References)
* [7 External links](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#External_links)
* [8 See also](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#See_also)

**Structural characteristics of the TCR**

The TCR is a disulfide-linked membrane-anchored heterodimer normally consisting of the highly variable alpha (α) and beta (β) chains expressed as part of a complex with the invariant [CD3](http://en.wikipedia.org/wiki/CD3_(immunology)) chain molecules. T cells expressing this receptor are referred to as α:β (or αβ) T cells, though a minority of T cells express an alternate receptor, formed by variable gamma (γ) and delta (δ) chains, referred as γδ T cells.[[2]](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#cite_note-Janeway_Immunobiology_-_Glossary-2)

Each chain is composed of two extracellular domains: Variable (V) region and a Constant (C) region, both of [Immunoglobulin superfamily](http://en.wikipedia.org/wiki/Immunoglobulin_superfamily) (IgSF) [domain](http://en.wikipedia.org/wiki/Immunoglobulin_domain) forming antiparallel [β-sheets](http://en.wikipedia.org/wiki/Beta_sheet). The Constant region is proximal to the cell membrane, followed by a transmembrane region and a short cytoplasmic tail, while the Variable region binds to the peptide/MHC complex.

The variable domain of both the TCR α-chain and β-chain each have three hypervariable or [complementarity determining regions](http://en.wikipedia.org/wiki/Complementarity_determining_region) (CDRs), whereas the variable region of the β-chain has an additional area of hypervariability (HV4) that does not normally contact antigen and, therefore, is not considered a CDR.

The residues are located in two regions of the TCR, at the interface of the α- and β-chains and in the β-chain [framework region](http://en.wikipedia.org/wiki/Framework_region) that is thought to be in proximity to the CD3 signal-transduction complex.[[3]](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#cite_note-pmid10318939-3) CDR3 is the main CDR responsible for recognizing [processed antigen](http://en.wikipedia.org/wiki/Antigen_processing), although CDR1 of the alpha chain has also been shown to interact with the [N-terminal](http://en.wikipedia.org/wiki/N-terminal) part of the antigenic peptide, whereas CDR1 of the β-chain interacts with the [C-terminal](http://en.wikipedia.org/wiki/C-terminal) part of the peptide.

CDR2 is thought to recognize the MHC. CDR4 of the β-chain is not thought to participate in antigen recognition, but has been shown to interact with [superantigens](http://en.wikipedia.org/wiki/Superantigen).

The constant domain of the TCR domain consists of short connecting sequences in which a cysteine residue forms disulfide bonds, which forms a link between the two chains.

**Generation of the TCR diversity**

Processes for the generation of TCR diversity are similar to those described for [B cell antigen receptors](http://en.wikipedia.org/wiki/B_cell_receptor), otherwise known as [immunoglobulins](http://en.wikipedia.org/wiki/Immunoglobulin). It is based mainly on somatic recombination of the DNA encoded segments in individual T cells.

TCRs possess unique antigen specificity, determined by the structure of the antigen-binding site formed by the α and β chains.[[4]](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#cite_note-Janeway_Immunobiology_-_TCR_Generation-4)

* The TCR *alpha chain* is generated by [VJ recombination](http://en.wikipedia.org/wiki/V(D)J_recombination), whereas the *beta chain* is generated by VDJ recombination (both involving a somewhat random joining of gene segments to generate the complete TCR chain).
* Likewise, generation of the TCR *gamma chain* involves VJ recombination, whereas generation of the TCR *delta chain* occurs by VDJ recombination.

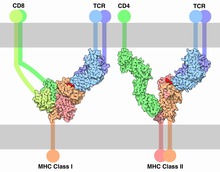
The intersection of these specific regions (V and J for the alpha or gamma chain; V, D, and J for the beta or delta chain) corresponds to the CDR3 region that is important for peptide/MHC recognition (see above).

It is the unique combination of the segments at this region, along with [palindromic](http://en.wikipedia.org/wiki/Palindromic) and random nucleotide additions (respectively termed "P-" and "N-"), which accounts for the great diversity in specificity of the T cell receptor for processed antigen.

**The TCR complex**

The TCR receptor complex is an octomeric complex of variable TCR receptor α and β chains with three dimeric signaling modules [CD3](http://en.wikipedia.org/wiki/CD3_receptor)δ/ε, CD3γ/ε and [CD247](http://en.wikipedia.org/wiki/CD247) ζ/ζ or ζ/η. Ionizable residues in the transmembrane domain of each subunit form a polar network of interactions that hold the complex together.[[5]](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#cite_note-pmid12507424-5) Since the [cytoplasmic](http://en.wikipedia.org/wiki/Cytoplasmic) tail of the TCR is extremely short, making it unlikely to participate in signaling, these signaling molecules are vital in propagating the signal from the triggered TCR into the cell.

Each T cell express clonal TCR which recognize specific peptide/MHC complex during physical contact between T cell and [antigen-presenting cell](http://en.wikipedia.org/wiki/Antigen-presenting_cell)-APC ([MHC class II](http://en.wikipedia.org/wiki/MHC_class_II)) or any other cell type ([MHC class I](http://en.wikipedia.org/wiki/MHC_class_I)) [[6]](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#cite_note-pmid19132916-6) High on-rate and off-rate is characteristic for TCR and peptide/MHC interaction at physiological temperature. TCRs have very high degree of antigen specifity, despite of fact that the affinity to the peptide/MHC ligand is in the micromolar range.[[7]](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#cite_note-pmid17082606-7) This weak binding (K_D dissociation constant values) between TCR and peptide/MHC was determined by the [surface plasmon resonance](http://en.wikipedia.org/wiki/Surface_plasmon_resonance)(SPR) to be in the range 1-100 μM, the association constant in the range from 1000 to 10000  M−1×s−1,[[8]](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#cite_note-pmid17442956-8) The TCR affinity for peptided/MHC has a direct impact on modulation of T cell function. T cell are very sensitive to their antigens despite the low affinity of TCR for its peptide/MHC and low numbers of specific peptide/MHC an the surface of target cells.[[9]](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#cite_note-pmid21365321-9) The specific and efficient signaling via TCR might be regulated by dynamic oligomerization into TCR microclusters on the surface of T cell.[[10]](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#cite_note-pmid23278737-10) In this scenario, T cell sensitivity to antigen could be increased via [avidity](http://en.wikipedia.org/wiki/Avidity)-based mechanism. The antigen sensitivity is higher in antigen-experienced T cells than in naive T cells. Naive T cells pass through the process of functional avidity maturation with no change in affinity. It is based on fact that effector amd memory (antigen-experienced) T cell are less dependent on costimulatory signals and higher antigen concentration than naive T cell.[[11]](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#cite_note-pmid22611418-11)

[](http://en.wikipedia.org/wiki/File:63-T-CellReceptor-MHC.tif)

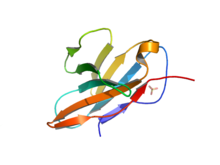
T-Cell Receptor complexed with MHC I and II

**TCR co-receptors**

The signal from the T cell complex is enhanced by simultaneous binding of the MHC molecules by a specific [co-receptor](http://en.wikipedia.org/wiki/Co-receptor).

* On [helper T cells](http://en.wikipedia.org/wiki/Helper_T_cells), this co-receptor is [CD4](http://en.wikipedia.org/wiki/CD4) that is specific for [MHC class II](http://en.wikipedia.org/wiki/MHC_class_II).
* On [cytotoxic T cells](http://en.wikipedia.org/wiki/Cytotoxic_T_cells), this co-receptor is [CD8](http://en.wikipedia.org/wiki/CD8) that is specific for [MHC class I](http://en.wikipedia.org/wiki/MHC_class_I).

The co-receptor not only ensures the specificity of the TCR for an antigen but also allows prolonged engagement between the [antigen-presenting cell](http://en.wikipedia.org/wiki/Antigen-presenting_cell) and the T cell and recruits essential molecules (e.g., [LCK](http://en.wikipedia.org/wiki/Lck)) inside the cell involved in the signaling of the activated T lymphocyte.

[](http://en.wikipedia.org/wiki/File:Homo_sapiens_CD8_molecule.png)

**Crystal structure of human CD8 molecule** Only a fragment of extracellular portion of human CD8α is shown. Co-receptor CD8 bind class I MHC specifically

**Associated molecules of the TCR complex involved in T-cell activation**

The essential function of the TCR complex is to identify specific bound antigen and elicit a distinct and critical response. The mechanism by which a T-cell elicits this response upon contact with its unique antigen is termed T-cell activation. There are myriad molecules involved in the complex biochemical process by which this occurs, which, in a wider context, is, in general, termed trans-membrane signalling.

The most common mechanism for activation and regulation of molecules beneath the lipid bilayer is via phosphorylation/dephosphorylation by protein kinases. T-cells utilise the [Src family kinases](http://en.wikipedia.org/wiki/Src_family_kinase) in transmembrane signalling largely to phosphorylate tyrosines that are part of [immunoreceptor tyrosine-based activation motifs](http://en.wikipedia.org/wiki/Immunoreceptor_tyrosine-based_activation_motif) (ITAM) in intracellular parts of CD3 and ζ chains.[[12]](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#cite_note-pmid17356173-12)

Early signaling steps implicate the following kinases and phosphatases after TCR triggering:

* [Lck](http://en.wikipedia.org/wiki/Lck) – [Src family kinase](http://en.wikipedia.org/wiki/Src_family_kinase) associated with the intracellular tail of CD4 and phosphorylate ITAMs
* [Fyn](http://en.wikipedia.org/wiki/Fyn) – [Src family kinase](http://en.wikipedia.org/wiki/Src_family_kinase) phosphorylate ITAMs of the CD3 and ζ ITAMs of the TCR complex
* [CD45](http://en.wikipedia.org/wiki/CD45) – The intracellular tail function as a tyrosine phosphatase activating Src family kinases
* [Zap70](http://en.wikipedia.org/wiki/Zap70) – Syk family kinase bind to ITAM sequences upon tyrosine phosphorylation by Lck and Fyn and phosphorylate LAT

When a T cell receptor is activated by contact with a peptide:MHC complex, CD45 dephosphorylates inhibitory tyrosine of membrane-localized [Src family kinases](http://en.wikipedia.org/wiki/Src_family_kinase) Fyn and Lck, previously recruited and activated by CD4 or CD8 coreceptors. Activated Fyn and Lck phosphorylates ITAMs on the CD3 and ζ chains. This allows cytoplasmic kinases of the Syk family (ZAP-70) to bind to the ITAM and activated ZAP-70 phosphorylates tyrosines on the adaptor protein [LAT](http://en.wikipedia.org/wiki/Linker_of_activated_T_cells), which then attracts PLC-γ. Other downstream pathways are triggered as well ([MAPK](http://en.wikipedia.org/wiki/Mitogen-activated_protein_kinase), [NF-κB](http://en.wikipedia.org/wiki/NF-%CE%BAB), [NFAT](http://en.wikipedia.org/wiki/NFAT)) which results in gene transcription in the nucleus.[[13]](http://en.wikipedia.org/w/index.php?title=T-cell_receptor&printable=yes#cite_note-13)

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**External links**

* [T-cell Group – Cardiff University](http://www.tcells.org/scientific/abTCR/)
* [UMich Orientation of Proteins in Membranes](http://en.wikipedia.org/wiki/Orientations_of_Proteins_in_Membranes_database) [*protein/pdbid-2hac*](http://opm.phar.umich.edu/protein.php?pdbid=2hac) – Zeta-zeta dimer of T cell receptor
* [T-Cell Receptor](http://www.nlm.nih.gov/cgi/mesh/2011/MB_cgi?mode=&term=T-Cell+Receptor) at the US National Library of Medicine [Medical Subject Headings](http://en.wikipedia.org/wiki/Medical_Subject_Headings) (MeSH)

**See also**

* [T cell](http://en.wikipedia.org/wiki/T_cell)
* [ImmTAC](http://en.wikipedia.org/wiki/ImmTAC)
* [Co-stimulation](http://en.wikipedia.org/wiki/Co-stimulation)
* [MHC multimer](http://en.wikipedia.org/wiki/MHC_multimer)

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* [Genes on chromosome 14](http://en.wikipedia.org/wiki/Category:Genes_on_chromosome_14)
* [Genes on chromosome 7](http://en.wikipedia.org/wiki/Category:Genes_on_chromosome_7)
* [Cell signaling](http://en.wikipedia.org/wiki/Category:Cell_signaling)
* [T cells](http://en.wikipedia.org/wiki/Category:T_cells)
* [Integral membrane proteins](http://en.wikipedia.org/wiki/Category:Integral_membrane_proteins)
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