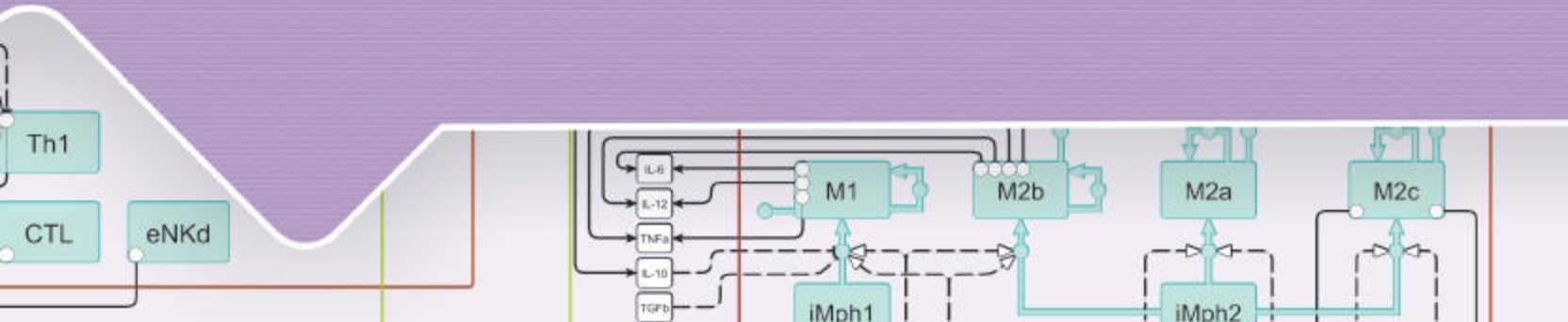
ISB[M]

Immune Response Template

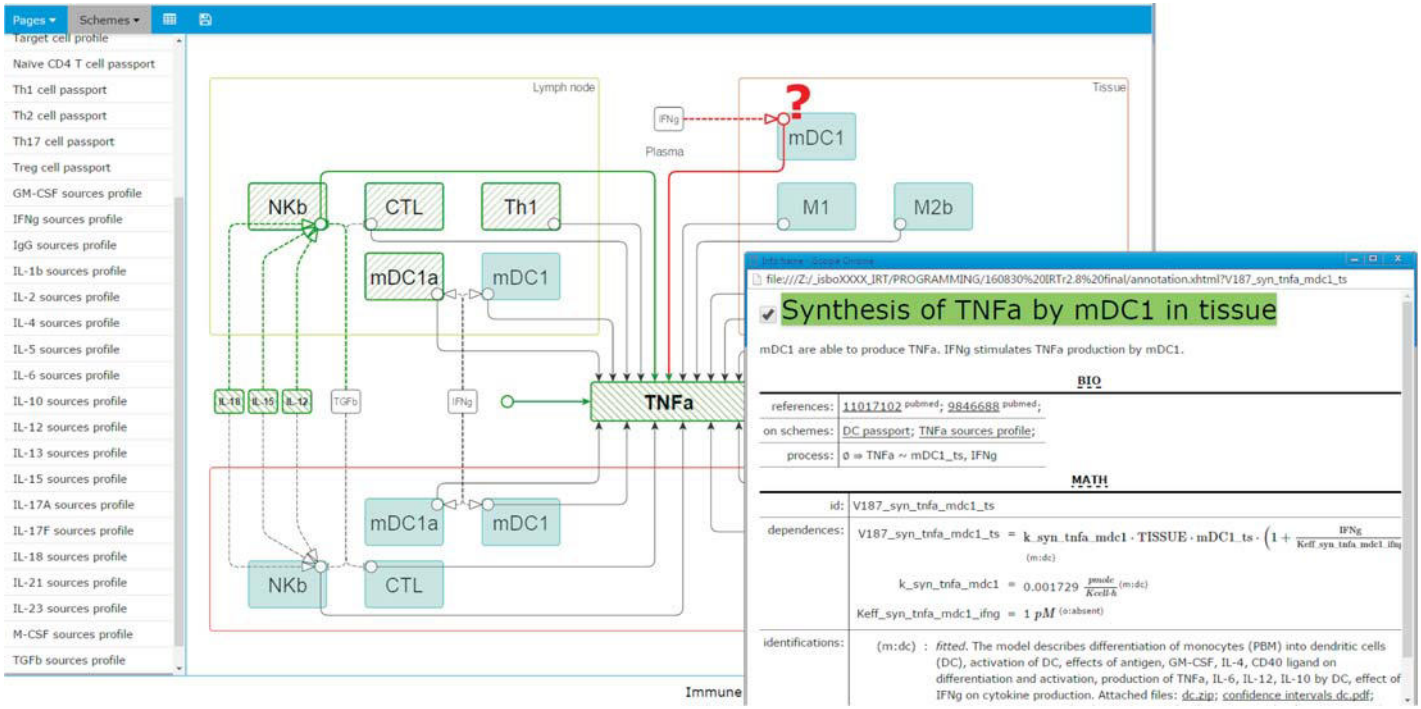


Institute for Systems Biology presents Immune Response Template

If you are interested in purchasing a license of the product, collaboration or partnering with ISBM for IRT development, please visit project page irt.insysbio.ru or send your request to irt@insysbio.ru

ISB[M]
Institute for Systems Biology Moscow

IRT navigator



ISB[M]
Institute for Systems Biology Moscow

About Immune Response Template

Immune Response Template (IRT) is a tool for development of QSP models of different diseases associated with immune response in human. Currently IRT consist of the database and the navigator.

The recent release of **IRT database 1.0** includes:

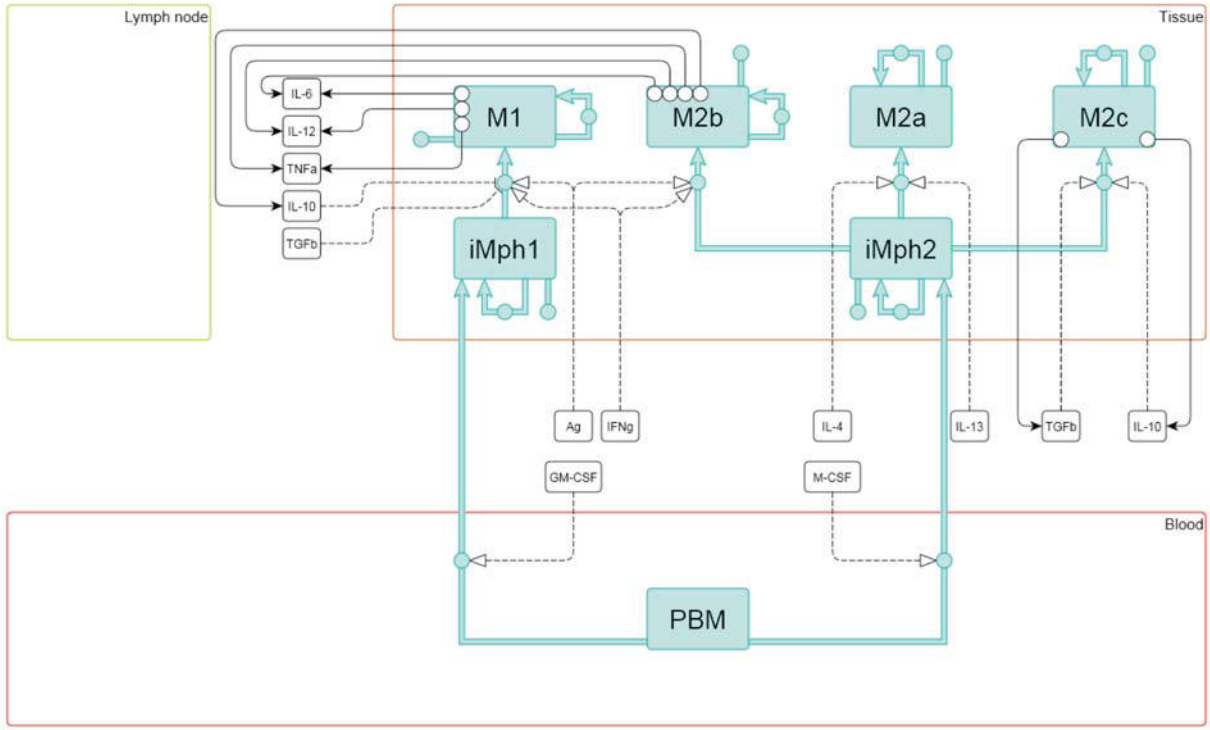
- interactive schemes (passport of immune cell and cytokine source profile) for database navigation;
- annotation of each process, cell and cytokine with cross references and links to the external databases;
- rate equations of key processes involved in immune response derived on the basis of existing knowledge;
- values of parameters of the rate equations identified via fitting of the specific “in vitro models” against in vitro data or calculated using in vivo data measured for healthy human;
- extended annotation of rate equations and parameters.

IRT navigator provides the intuitive interface for searching the information and model template creation:

- visualization of description and annotation of IRT database components: equations, species, parameters;
- access to supplementary materials including files related to in vitro models, files with description of parameters calculation;
- navigation across multiple interactions of immune cells;
- automatic generation of model template based on the user selection which can be downloaded as fully annotated SBML file.

ISB[M]
Institute for Systems Biology Moscow

Passport of macrophages



ISB[M]
Institute for Systems Biology Moscow

Passports of immune cells

"Passport" of immune cell is a scheme visualizing literature available experimental facts on:

- activation, differentiation and proliferation of the cell;
- migration of the cell between blood, lymph node and tissue;
- cytokines which are synthesized by this type of cell upon activation;
- cytokines or cells that affect this type of cell.

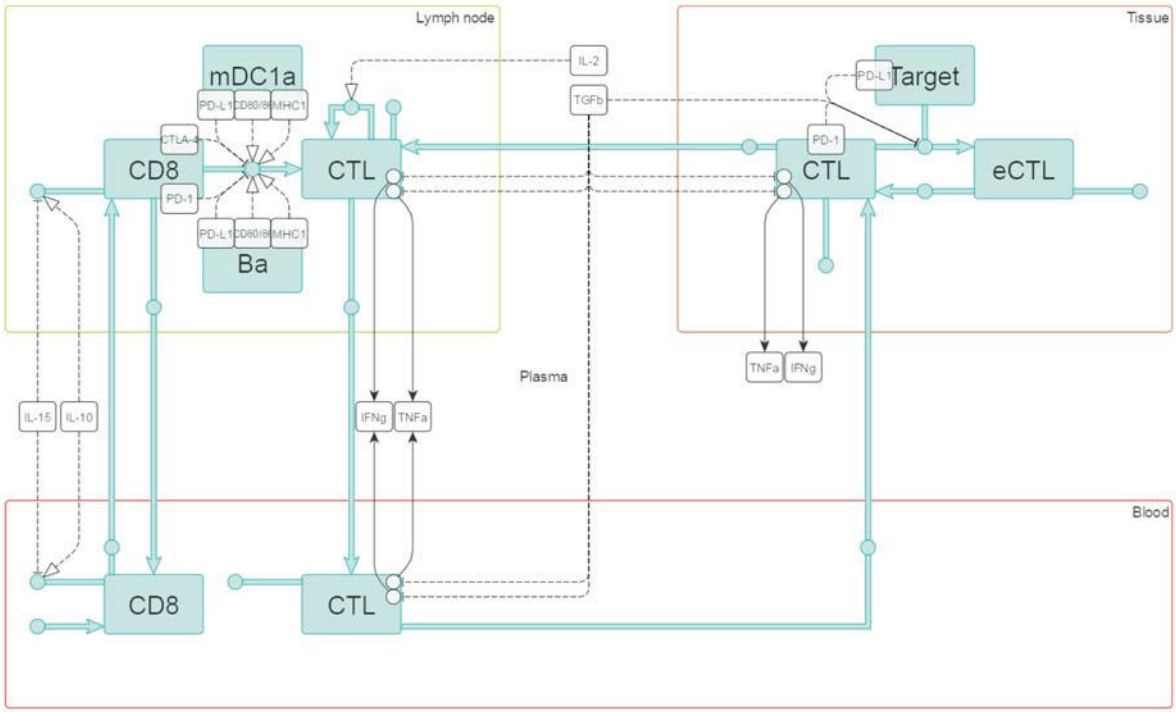
IRT database 1.0 includes passports of the cells presented in the table.

Cell	NK	DC	Mph*	PBM**	MDSC	B cells	Th0***	Th1	Th2	Th17	Treg	Naïve CD8 T cells/CTL
Passports	+	+	+	+	+	+	-§	+	+	+	+	+
Rate equations	+	+	+	+	-	+	+§§	+	+	+	+	+
Identified parameters	+	+	+	+	-	+	+§§	+	+	+	+	+

**Macrophages; **Peripheral Blood Monocytes; ***Naïve CD4 T cells; §Th0 cells are presented in cytokine passports of Th1, Th2, Th17 and Treg cells. §§Th0 sub-model describes only Th0 apoptosis in vitro; Th0 differentiation into Th1, Th2, Th17 and Treg cells is described in Th1, Th2, Th17 and Treg sub-models.*

ISB[M]
Institute for Systems Biology Moscow

Passport of CD8 T cells



ISB[M] Institute for Systems Biology Moscow

Surface molecules on passport

Immune cells can directly interact to each other via binding of their surface molecules. A set of the surface molecules regulating the immune response were included into cell passports.

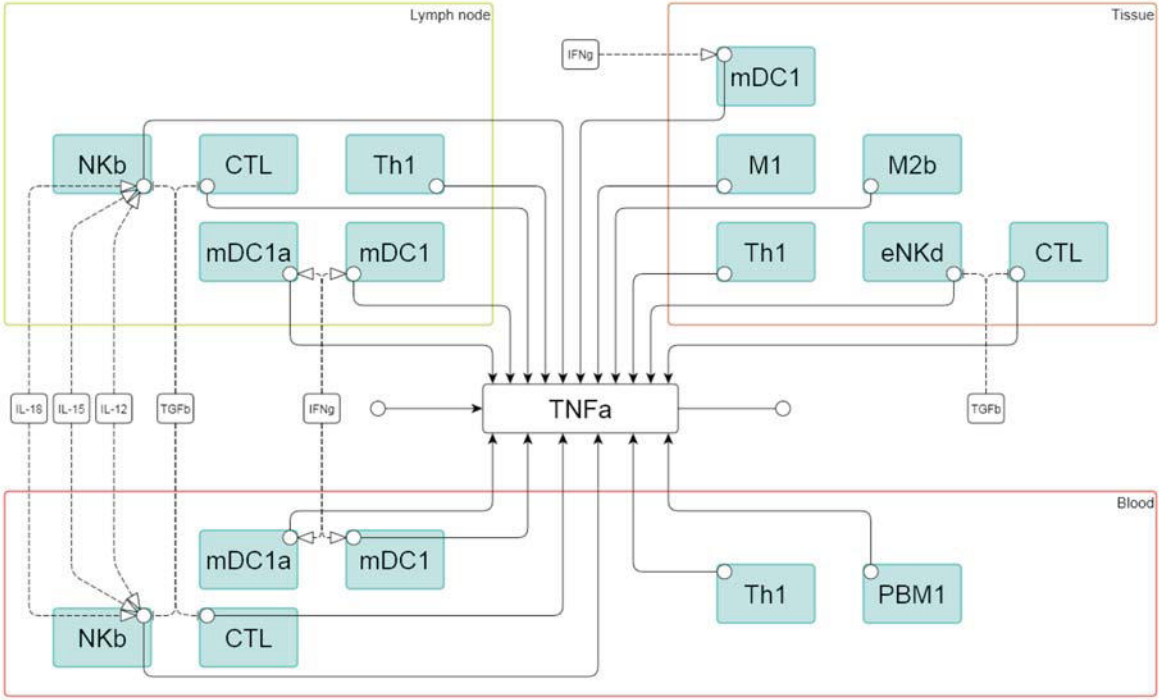
For each process describing direct cell-cell interactions rate equation were derived in such a way to take into account binding of corresponding surface molecules.

Surface molecules included in IRT database 1.0 are described in table.

Surface molecules	CD3 (Implicitly)	MHC-I	MHC-II	CD28 (Implicitly)	CTLA-4	CD80/86	PD-1	PD-L1	CD40L	CD40 (Implicitly)
Rate equations	+	+	+	+	+	+	+	+	+	+

ISB[M]
Institute for Systems Biology Moscow

TNFα source profile



ISB[M] Institute for Systems Biology Moscow

Cytokine sources profile

Cytokine source profile is a scheme visualizing literature available experimental facts on

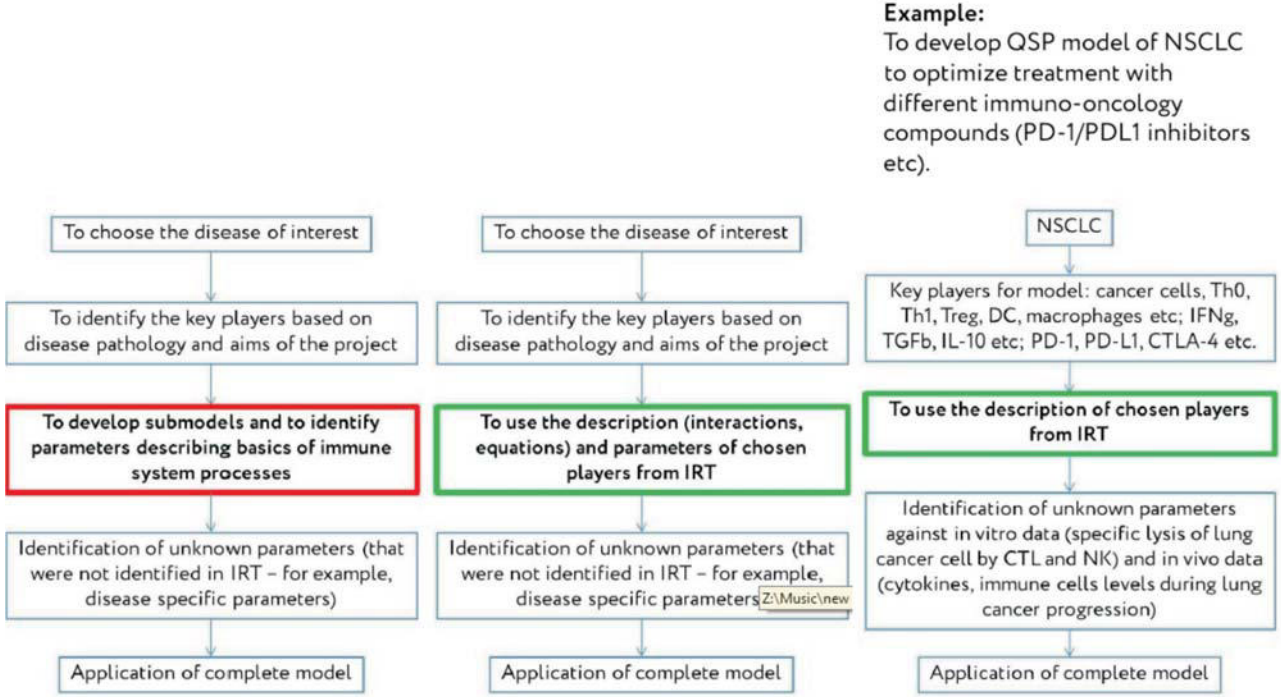
- production of the cytokine by different immune cells located in blood, lymph node and tissue
- regulation of production of the cytokine by other cytokines

Cytokines included in IRT are described in table.

Cytokine	GM-CSF	M-CSF	IFNγ	TNFα	TGFβ	IL-1β	IL-2	IL-4	IL-5	IL-6	IL-10	IL-12	IL-13	IL-15	IL-17	IL-18	IL-21	IL-23
Rate equations	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Identified parameters	+	-	+	+	-	-	+	+	-	+	+	+	-	+	-	-	-	-

ISB[M] Institute for Systems Biology Moscow

Application of IRT for model development



ISB[M] Institute for Systems Biology Moscow

Further steps of IRT development

- To implement database infrastructure which allows

  - to populate IRT in semi-automatic manner and as a result to decrease probability of typing errors
  - to collect, store and reproduce digitized data taken from public sources

- To include more mechanistic details in description of players (cells, cytokines, surface molecules) that are already included in IRT

- To add description of new

  - types of cells: eosinophil, neutrophil, mast cell, basophil, microglia, fibroblast etc.
  - cytokines: IL-1α, IL-22, IL-8, TSLP, IL-33, IL-12, IFNα etc.
  - surface molecules: LAG3, GITR, NKG2A, KIR, 4-1BB etc.
  - chemokines: IP-10, MIP-1α, MIP-1β, BLC, ELC etc.
  - molecules related to cancer immunology: IDO1, TDO etc.
  - compartments (organs): liver, brain, lung etc.

ISB[M]
Institute for Systems Biology Moscow

Demo version

The demo package of IRT is available for free.

Demo includes:

- IRT navigator with complete functionality;
- IRT database 1.0 limited to: Th2 cells passport; IL-4 sources profile; IL-5 sources profile

To get demo version of IRT please send your request to
email: insysbio@insysbio.ru
website: irt.insysbio.ru