



CYTOGNOS RESPONSE TO COVID-19

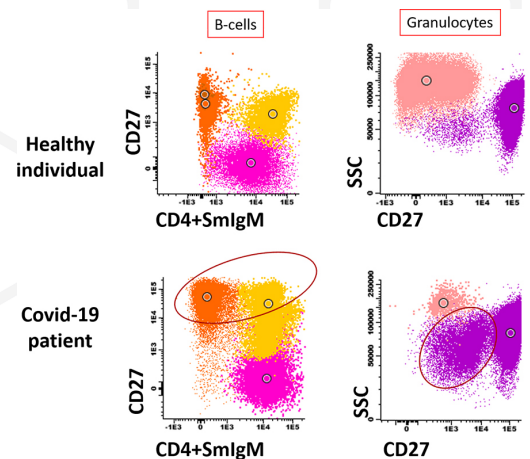
IMMUNE MONITORING OF COVID-19 PATIENTS

Immune monitoring of COVID-19 patients allows us to study in depth their immune status which can provide prognostic value in terms of recovery dynamics. Therefore, clinical and therapeutic decisions based on this knowledge result in better and more personalized care for patients.

The PIDOT and IgH-Isotype panels have been designed by the EuroFlow™ consortium and are included within a perfectly tested, validated and standardized methodology.

The complete standardization of the methodology allows for the use of reference age-related databases with numeric and immunophenotypic data from healthy donors. The analysis and automatic reporting provided by the Infinicyt™ software permits a powerful and visual evaluation of all lymphocyte subpopulations for a better understanding of the immune context of the patient.

The major advantage of this approach is that it facilitates faster and standardized immune monitoring of COVID-19 patients and allows for a full exchange of data between different laboratories worldwide.



THE EUROFLOW™ PID ORIENTATION TUBE

PATENTED!

BV™421*	BV™510*	FITC	PE	PerCP-Cyanine5.5	PE-Cyanine7	APC	APC-C750
CD27	CD45RA	CD8+SmlgD	CD16+CD56	CD4+SmlgM	CD19+TCRγδ	CD3	CD45

*Not included in the PIDOT kit. Should be added as drop-ins.

The PIDOT is a single 8-color tube developed for identification of the main lymphocyte subsets. It can be used in combination with novel Infinicyt™ tools in order to optimize immunophenotypic evaluation of immune cells.

With this combination, lineage specific identification markers (CD3, CD19, CD16+CD56), total T, B and NK cells can be identified. Subsequently using functional (CD4, CD8, TCRgd, IgM, IgD) and maturation (CD27 and CD45RA) specific markers, T and B cell subsets with diagnostic value can be identified: T-helper, T-cytotoxic and their naïve, memory and effector stages, and pre-germinal center (GC), post-GC, Ig class unswitched and switched B cells.

EMBRACE NEXT GENERATION FLOW

A COMPLETE SOLUTION FROM SAMPLE PREPARATION TO EXPERT-GUIDED AUTOMATED REPORTING

This EuroFlow™ PIDOT combination is patent protected and has been evaluated in several multicenter rounds. Each specific clone-fluorochrome combination was selected to provide an optimal performance using the standardized EuroFlow™ protocols.

This optimized PIDOT combination is produced by Cytognos as a pre-mixed lyophilized reagent, stable and reproducible for long periods of time, and compatible with the automated gating and identification tool implemented in the Infinicyt™ analysis software.

Population	Hospitalization		Day+7	
	Cells/μl	Reference (cells/μl)	Cells/μl	Reference (cells/μl)
Lymphocytes	1152	(1231 - 3787)	1448	(1231 - 3787)
B cells	135	(61 - 394)	156	(61 - 394)
Pre-germinal center	46	(28.9 - 278)	91.8	(28.9 - 278)
Post-germinal center	89.3	(21.6 - 171)	64.7	(21.6 - 171)
Unswitched MBC/PC	42.2	(12.5 - 102)	39.8	(12.5 - 102)
Switched MBC/PC	47.1	(10.2 - 77.6)	24.4	(10.2 - 77.6)
IgD+IgM- postGC	0	-	0.38	-
T cells	570	(907 - 2576)	1058	(907 - 2576)
CD4+CD8-	290	(446 - 1694)	687	(446 - 1694)
CD4+ Naïve	111	(80.3 - 1000)	308	(80.3 - 1000)
CD4+ Central/Transitional Memory	122	(237 - 771)	291	(237 - 771)
CD4+ Effector Memory	38.8	(25.1 - 401)	30.2	(25.1 - 401)
CD4+ Effector TD	18.5	(0 - 627)	57	(0 - 627)
CD8+CD4-	244	(173 - 1463)	339	(173 - 1463)
CD8+ Naïve	15.2	(20.4 - 293)	85	(20.4 - 293)
CD8+ Central/Transitional Memory	50.2	(62.1 - 451)	100	(62.1 - 451)
CD8+ Effector Memory	21.7	(4.2 - 358)	0.056	(4.2 - 358)
CD8+ Effector TD CD27+d	3.8	(5.4 - 287)	39.7	(5.4 - 287)
CD8+ Effector TD CD27-	153	(0 - 641)	114	(0 - 641)

IgH-ISOTYPE PANELS - SUBCLASSES

PATENTED!

Compatible with 12-color panels

	FITC	PE
Tube 1	IgG2 IgG4	IgG1 IgG2
Tube 2	IgA1 IgG3	IgA1 IgA2

Compatible 8-color panels

FITC	PE	PerCP-Cyanine5.5	APC
IgG2 IgG3	IgG1 IgG2	IgA1 IgA2	IgA1 IgG4

The IgH-Isotype subclasses tube was designed to analyze the status of the B-cell and plasma cell compartment. During infection or after vaccination, dynamic changes can be observed at a cellular level for total numbers and relative distribution of the B compartment in peripheral blood.

Age-related reference values are available when using this IgH-isotype B-cell tube together with CD27, IgM, CD21, CD24, CD19, SmlgD, CD5, CD38.

- Specific IgG and/or IgA subclasses response can be identified after infection or vaccination, showing insight of the immunity to new viral infection.
- Response to vaccination can be predicted in patients with reduced ability to produce antigen-specific antibodies.
- The evaluation of plasma cell counts can be used as a surrogate marker for their future production in bone marrow.

EuroFlow™ has designed two versions of the IgH-Isotype panel, adapted to 8-color and 12-color flow cytometers, which differ on the fluorochrome-marker combinations and the number of tubes used.

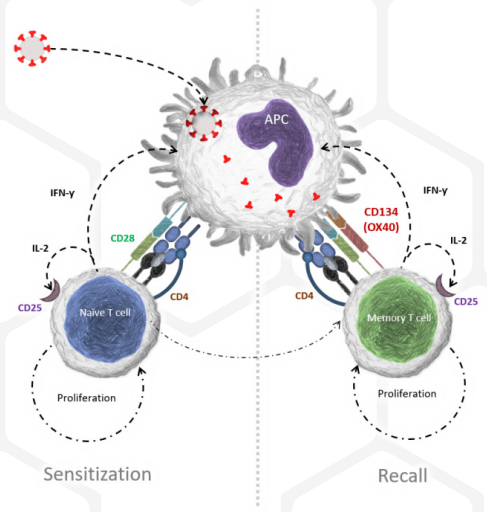
EMBRACE NEXT GENERATION FLOW

A COMPLETE SOLUTION FROM SAMPLE PREPARATION TO EXPERT-GUIDED AUTOMATED REPORTING

MONITORING OF CELLULAR IMMUNE RESPONSE AGAINST SARS-COV-2 INFECTION

The OX40 assay can be applied for the study of the immune response mediated through CD4 T-cells after contact with pathogens, such as SARS-CoV-2 in healthy and infected individuals.

- The usefulness of antibody tests as a diagnostic method is limited given that their sensitivity in the first week post-infection is low, but they are key for seroprevalence and immunization studies.
- The absence or decrease of antibody levels cannot be considered as a lack of immunity since it is possible to generate cellular immune memory with T lymphocytes.
- The CD4 antigen-specific memory T-cells are activated with renewed contact with the antigen within the organism. This subpopulation can be detected with the Act-T4 Cell™ kit combined with the use of specific viral proteins for incubation.



Act-T4 Cell™ KIT

FITC	PE	PerCP-Cyanine5.5	APC
CD4	CD134	CD3	CD25

PATENTED!

APPLICATIONS



Prevalence studies

Combination of antibody tests and specific T-cell responses could improve current estimations:

- Not all individuals produce antibodies in response to the viral infection
- Antibody levels decay in peripheral blood along time



Immunization studies

Accurately estimate the extent and duration of immunization after infection or vaccination



Immunization of immunocompromised and immunodeficient individuals

The extent and efficacy of vaccine responses in immunocompromised (transplantation, autoimmunity and oncology) and immunodeficient (primary and secondary) individuals is currently unknown



Identification of vulnerable patients

Assessment of individuals at risk of reinfection for adequate planification of response and vaccination schemes

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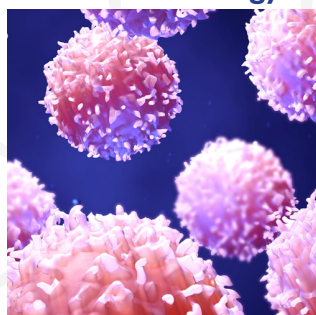
REFERENCES

1. Chen G, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. *Journal of Clinical Investigation*. 2020 May; 130(5):2620-9.
2. Cossarizza A, et al. SARS-CoV-2, the Virus that Causes COVID-19: Cytometry and the New Challenge for Global Health. *Cytometry Part A*. 2020 Apr; 97(4):340-3.
3. Wang F, et al. Characteristics of Peripheral Lymphocyte Subset Alteration in COVID-19 Pneumonia. *The Journal of Infectious Diseases*. 2020 May; 221(11):1762-9.
4. Zhang B, et al. Immune Phenotyping Based on the Neutrophil-to-Lymphocyte Ratio and IgG Level Predicts Disease Severity and Outcome for Patients With COVID-19. *Frontiers in Molecular Biosciences*. 2020 Jul; 7:157.
5. Zaunders J, et al. High levels of human antigen-specific CD4+ T cells in peripheral blood revealed by stimulated coexpression of CD25 and CD134 (OX40). *The Journal of Immunology*. 2019 Aug; 183(4):2827-36.
6. Phetsouphanh C, et al. Detecting Antigen-Specific T Cell Responses: From Bulk Populations to Single Cells. *International Journal of Molecular Sciences*. 2015 Aug; 16(8):18878-93.

Product	Reference	Format	Size
PIDOT kit	CYT-PIDOT	Lyophilized	20 test
IgH-Isotype Subclasses	CYT-IGS-1 / CYT-IGS-2	Lyophilized / Liquid	20 test
Act-T4 Cell™ KIT	CYT-AT4C	Liquid	100 test
Infinicyt™ Advanced License	CYT-INFINICYT-ADVANCED		
EuroFlow™ Database Accesses	CYT-INFINICYT-EFDB		

Flow Cytometry Solutions

Next Generation Flow™ solution for Oncohematology



Next Generation Flow™ solution for Immunology



Next Generation Flow™ solution for Clinical trials



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