GESINAS - ImmunoTools Award 2018

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Tumor microenvironment interactions of macrophages and malignant B-cells in human chronic lymphocytic leukemia

Chronic lymphocytic leukemia (CLL) is a disease defined by accumulating malignant B-cells, which continue to proliferate over a long period of time not following the fate of healthy B-cells. It has been postulated that the primary reason for this non-responsiveness to cell death signals and the limitless growth of the cells are due to tonic signaling of the B-cell receptor (BCR), which these cells exhibit. Our group has recently shown that not only the B-cells themselves drive the disease, but that cells in the micro-environmental niche of the lymph node, particularly tumor-associated macrophages (TAM) play a predominant role in the pathogenesis of the disease.

In order to assess the specific roles of both, malignant B cells and myeloid cells in their micro-environment we will employ co-culture systems with cells from different origins, primary and cell lines, of both cell types.

In particular we will assess the impact of kinase inhibitors targeting BCR signaling on the interaction of malignant B cells with myeloid cells. In co-cultures an excess of malignant B cells will be kept in cell culture medium together with monocytes or preferentially on a layer of differentiated macrophages.

In these co-cultures cell survival and proliferation will be monitored in both cell types, but emphasis will be placed on cell functions with importance for the micro-environmental dialogue, e.g. cytokine secretion, migration and adhesion.
For these investigation reagents supplied by ImmunoTools could be used for different purposes.

- Certain cytokines will be useful for stimulating CLL cells (sCD40L) or for polarizing macrophages (IL-4, IL-13, IFNγ, M-CSF, GM-CSF)
- Production of cytokines by both cell types alone or in co-culture will be monitored with the aid of ELISAs (CXCL12, CCL2, CCL3, IL-6, IL-8, IL-10)

- Moreover, fluorescence-labeled antibodies will allow to distinguish B-lymphoid (CD5, CD19) and myeloid cells (CD11a, CD14, CD33)
- The trans-well migration of THP-1 monocytes can be screened against a panel of chemo-attractants, consisting e.g. of CXCL8 (IL-8), CXCL12 (SDF-1), CCL2 (MCP-1), CCL3 (MIP-1α), CCL4 (MIP-1β) and CCL7. Similar assays could be performed with OSU-CLL cells using CXCL12, CCL19 or CCL21 as chemoattractants

Overall the ImmunoTools award would strongly improve the scope of how deep we aim to characterize the interaction between macrophages and malignant B-cells in the tumor microenvironment and enable us to explore this interaction on a broader scale.

GESINAS-Award application

Next to my studies I am co-organizing the CIO Summer Academy at the University Clinics of Cologne. Our program is designed for pupils at the end of their school education and offers them an opportunity to get first insights into the life of us researchers. The program consists of lectures held by PhD and Post-Doctoral scientist from all over the University Clinics, a four week practical training with one-on-one mentoring in various laboratories and of course some social events for the young, enthusiastic scientists-to-be. Personally, I am very happy to contribute to such a big project and it inspires me a lot to accompany these young people experience laboratory life – a field well known to me, but certainly new, and at times extraordinary, to them. So far we have received a lot of positive feedback from both sides, the students, as well as the lab-mentors and lecturers, stating that the way of scientific exchange we offer with this program is really unique.

References:

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GESINAS ImmunoTools AWARD for **Floyd Hassenrück** includes 40 reagents

FITC - conjugated anti-human: CD11a, Annexin V

PE - conjugated anti-human: CD14

PerCP - conjugated anti-human: CD5

APC - conjugated anti-human: CD19, CD33

recombinant human cytokines: Exodus-2, GM-CSF, IFNγ, IL-4, IL-8, IL-13, MCP-1, MCP-3, M-CSF, MIP-1α, MIP-1β, MIP-3b, SDF-1a

soluble human receptors: rh sCD40L / CD154

human ELISA-set (for one 96 plate): TNF-a, IFN-y, IL-6, IL-8, IL-10

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