

EFFECTOR RESPONSE

1. CLASSICAL EFFECTOR RESPONSE UNDERSTANDING

Cell death can occur by multiple molecular mechanisms. The information on how the cell dies is contained within the dead cell. Additionally, there may be information on whether the cell is infected or uninfected, and even about its specific identity. Let \mathcal{T} be the set of “*types of programmed cell deaths*”, let \mathcal{Id} be the set of “*identities of the dying cell*” and let \mathcal{O} be the set of “*other variables*”. Then, the set \mathcal{D} of “*cell deaths*” can be described formally as the Cartesian product

$$(1.1) \quad \mathcal{D} := \mathcal{T} \times \mathcal{Id} \times \mathcal{O}.$$

In other words, a type of “*programmed cell death*”, an “*identity of the dying cell*” and “*other variable*” completely characterize a type of “*cell death*”.

The simplest response to cell death is where death itself executes the programmed function and hence, classically the “*effector response*” is thought of directly as a function of “*cell death*”. Formally, if we denote by \mathcal{Eff} the set of “*effector responses*”, then a type of “*cell death*” was thought to give rise to exactly one type of “*effector response*” and thus could be described as a function

$$(1.2) \quad f : \mathcal{D} \mapsto \mathcal{Eff}.$$

That is, a type $d \in \mathcal{D}$ of “*cell death*” was thought to be assigned to a unique type of “*effector response*” $f(d) \in \mathcal{Eff}$.

2. NEW EFFECTOR RESPONSE UNDERSTANDING

The new proposition is that the classical understanding (1.2) of “*effector response*” as a function of “*cell death*” is incomplete because a type $d \in \mathcal{D}$ of “*cell death*” can be observed to give rise to multiple “*effector responses*” and can thus not be thought of formally as a function. However, if we take into account the environment of cell death and the specific efferocyte, then we propose a new understanding of “*effector responses*” as a function of these additional inputs. More precisely, if we denote by \mathcal{Env} the set of “*environments of cell death*” and by \mathcal{Effero} the set of “*specific efferocyte*” then we propose the following new understanding

$$(2.1) \quad f : \mathcal{D} \times \mathcal{Env} \times \mathcal{Effero} \mapsto \mathcal{Eff}$$

of “*effector response*” as a function of “*cell death*”, “*environments of cell death*” and “*specific efferocyte*”. In other words, a type $d \in \mathcal{D}$ of “*cell death*”, a type $x \in \mathcal{Env}$ of “*environments of cell death*” and a type $y \in \mathcal{Effero}$ of “*specific efferocyte*” give rise to a unique type $f(d, x, y) \in \mathcal{Eff}$ of “*effector response*”.

In some special cases, the environment and cell death can be constrained, for example pyroptosis and inflammation are obligatorily paired. The environment may also pre-specify the efferocyte available to recognize and dispose of the dead cell. These constraints can be taken into account by a simple extension of (2.1). Namely, there is a subset $\mathcal{A} \subset \mathcal{D} \times \mathcal{Env} \times \mathcal{Effero}$, which we refer to as the set of “*admissible combinations*”, for which the “*effector response*” can be understood as a function

$$(2.2) \quad f : \mathcal{A} \mapsto \mathcal{Eff}$$

of the set \mathcal{A} of “*admissible combinations*”. In other words, a type $d \in \mathcal{D}$ of “*cell death*”, a type $x \in \mathcal{Env}$ of “*environments of cell death*” and a type $y \in \mathcal{Effero}$ of “*specific efferocyte*” give rise to a unique type $f(d, x, y) \in \mathcal{Eff}$ of “*effector response*” if the triple $(d, x, y) \in \mathcal{A}$ is an “*admissible combination*”.