Cell death is a fundamental biological process, essential for maintaining tissue homeostasis. In healthy conditions, around one million cells die every second. When dysregulated, however, cell death becomes detrimental: excessive cell death drives inflammatory and degenerative diseases, while insufficient cell death is a hallmark of cancer. The Cell Death and Inflammation Unit aims to unravel both the cell-intrinsic and intercellular mechanisms of cell death and to explore their links with inflammation, neurodegeneration, and cancer.

“Our unit actively engages with the local and international research community in the fields of cell death and inflammation,” says group leader Professor Dr. Peter Vandenabeele. “With four teams focusing on interconnected aspects of these processes, we bring together a critical mass of expertise. A dynamic culture of discussion among team leaders and postdoctoral researchers strengthens our research and allows us to fill an important and complementary niche within the **VIB-UGent Center for Inflammation Research (IRC)**.”



The Cell Death and Inflammation Unit (June 2025). © Cell Death and Inflammation Unit

Research on cell death has a long-standing tradition at Ghent University (UGent) and has expanded considerably over the past decade. “Currently, we are establishing the local initiative **Cell Death Research – Ghent (CDR-G)**, which aims to integrate cell death research activities across more than 15 groups at UGent. The initiative will focus on sharing expertise and tools, organizing scientific meetings, increasing international visibility and recruitment, and coordinating collaborative projects. These groups cover a wide range of topics, including cell death in plants, the molecular biology of cell death,

and biomedical applications targeting cell death in inflammation, autoimmunity, and cancer." A dedicated website for CDR-G will launch by the end of 2025.

Part of the local and global cell death research community

The strength of the Ghent research hub is also reflected in **Expertscape** rankings. VIB-UGent and UGent are listed among the world's top 10 institutions in necroptosis and pyroptosis research, respectively. Individual researchers are also highly ranked in regulated cell death (#5), phagocytosis (#1), necroptosis (#8), pyroptosis (#3), and inflammasomes (#3) (as of 2025). "While we acknowledge the limitations of such rankings, they nevertheless highlight the presence of a strong and productive critical mass of researchers in Ghent dedicated to advancing the field of cell death."

A lively field in biomedical science

Peter Vandenabeele explains: "Billions of cells in the human body die every day. It is essential for maintaining tissue homeostasis and eliminating harmful cells. Cellular stress, infection, and inflammation can trigger different forms of cell death. Depending on the type of stimulus, the affected cell type, and the cellular environment, a variety of cell death outcomes may arise, sometimes even co-occurring within a single population of cells."

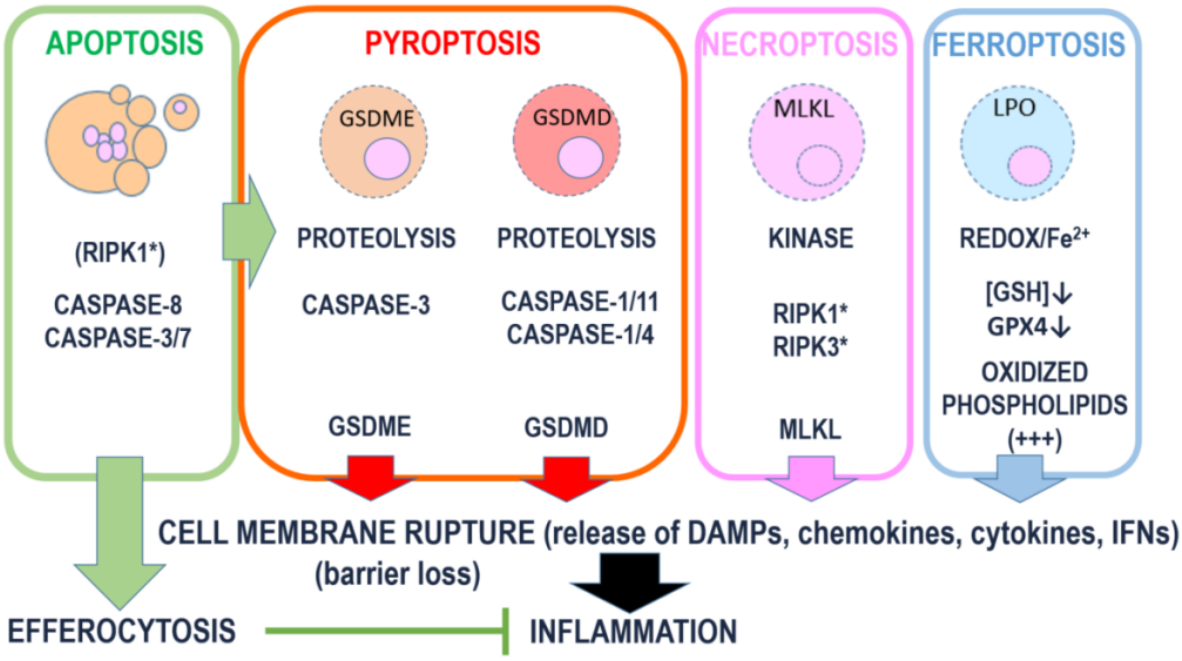


Figure 1. Many ways to die. © Cell Death and Inflammation Unit

The major forms of regulated cell death include **apoptosis, necroptosis, and**

pyroptosis, each driven by distinct genetically programmed mechanisms, as well as **ferroptosis**, a metabolically regulated form of cell death (Figure 1). Because of its far-reaching impact, the process of cell death must be tightly regulated. Excessive cell death is now recognized both as a major driver and a consequence of inflammatory pathologies. Inflammation itself plays a dual role: on one hand, it is crucial for host defence against microbial pathogens and for tissue repair after sterile injury; on the other, when uncontrolled, it becomes harmful, driving tissue damage, organ dysfunction, and the progression of numerous acute and chronic diseases.

“Despite significant advances, our understanding of how protective inflammation transitions into pathological inflammation remains incomplete. A deeper knowledge of the molecular and cellular pathways that regulate the intensity, duration, and resolution of inflammation is needed (Figure 2). By studying the regulation of cell death, whether through signalling cascades or perturbations of metabolic networks, we can identify tangible therapeutic strategies. These may allow us to enhance or suppress cell death processes and their associated signalling programs in a wide range of diseases, including cancer, ischemia-reperfusion injury, inflammatory disorders, and degenerative diseases.”

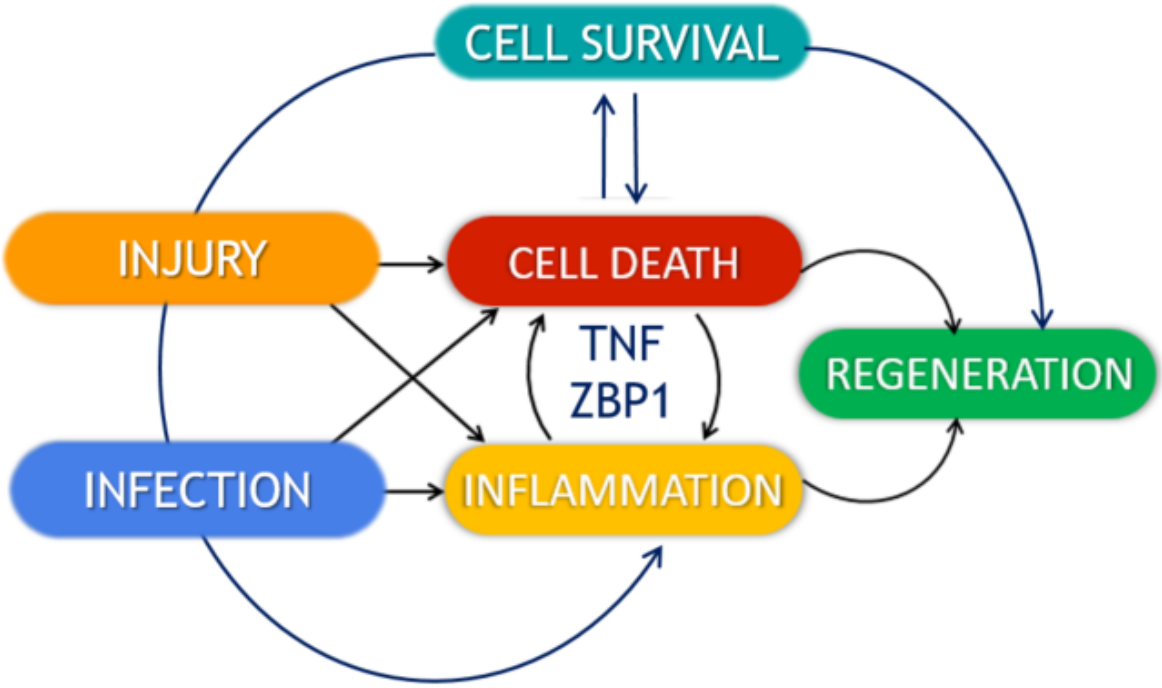


Figure 2. Cell death and inflammation are interconnected. © Cell Death and Inflammation Unit

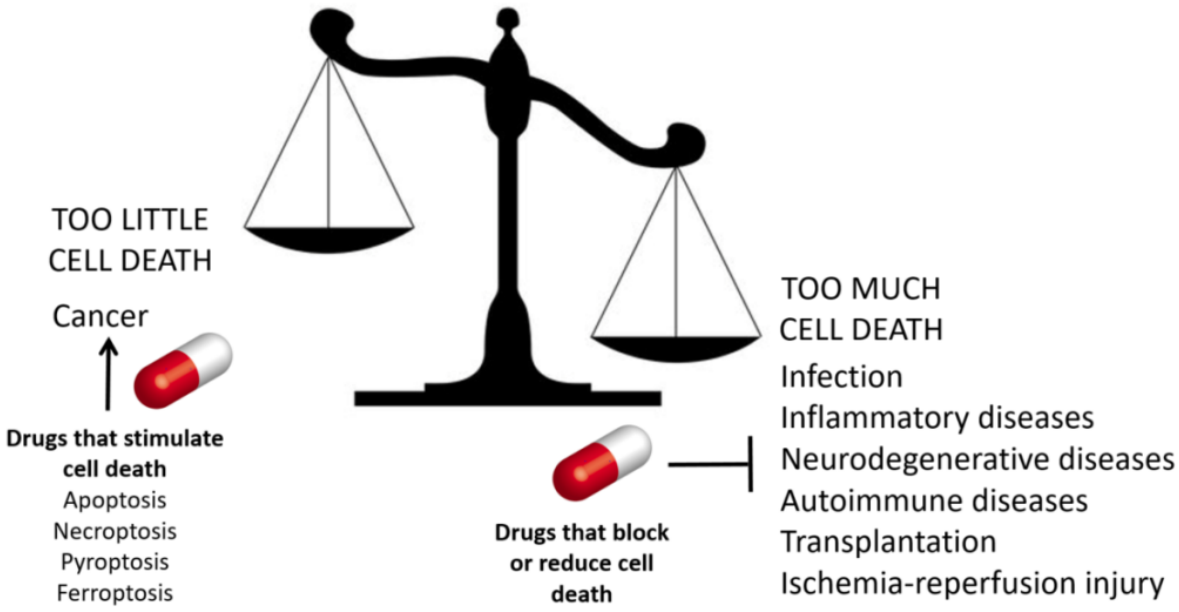


Figure 3. Many diseases are connected with cell death, either too much or too little. © Cell Death and Inflammation Unit

Too much or too little cell death

Targeting cell death is highly relevant across a wide spectrum of diseases, which can often be characterized by either excessive or insufficient cell death (Figure 3). “For example, **chronic inflammatory diseases** such as rheumatoid arthritis, Crohn’s disease, psoriasis, atherosclerosis, and type II diabetes are partially driven by excessive cell death, which amplifies inflammation. Similarly, conditions including **sepsis, organ failure, neurodegenerative diseases,** and complications in **organ transplantation** are also associated with increased cell death. In these cases, therapeutic strategies that prevent, block, reduce, or delay the cell death process may prove beneficial. Conversely, in **cancer**, cells often escape death by suppressing or disabling cell death pathways, either through silencing pro-death genes or activating survival genes. Here, therapeutic strategies focus on reactivating or sensitizing alternative cell death programs to bypass these blocks, enabling targeted elimination of malignant cells.”

Peter Vandenabeele continues: “Because cell death results in the loss of cells and the energy invested in building them, its regulation must be extremely precise. At the *Cell Death and Inflammation Unit*, our main objective is to advance fundamental knowledge on both cell-intrinsic and intercellular aspects of cell death as a major driver of inflammation. Our research focuses on unravelling molecular checkpoints that determine life-or-death decisions, as well as adaptive responses triggered by triggered by cytokines

(in this case, **Tumor Necrosis Factor – TNF**), nucleic acids (in this case, **Z-DNA-binding protein 1 – ZBP1**), and metabolic cell death by **ferroptosis**. We study these mechanisms in experimental disease models of cancer, systemic inflammatory response syndrome (SIRS), intestinal disorders, and skin diseases."

Research focus

The Cell Death and Inflammation Unit brings together four research teams, each addressing distinct but interconnected aspects of regulated cell death and its impact on inflammation, cancer, infection, and immune regulation. Together, these teams aim to generate fundamental insights into cell death mechanisms and translate them into therapeutic strategies.

Vandenabeele Team – Immunogenic Cell Death & Cancer Immunotherapy

Focus: How to render ferroptosis immunogenic to enhance cancer immunotherapy.
Key Findings: Ferroptosis, a cell death process driven by iron-dependent lipid peroxidation (LPO) at the plasma membrane, induces strong immunosuppression in cancer cells by disrupting antigen cross-presentation by dendritic cells.

Research Goal: To dissect the role of lipid and redox metabolism networks in regulating ferroptosis sensitivity and immunogenicity, with the ultimate goal of developing strategies that boost the efficacy of immunotherapy and radiotherapy in experimental cancer models.

Declercq Team – Cell Death and Inflammation in the Skin & Carcinogenesis

Focus: Mechanisms that maintain skin homeostasis in health and disease.
Key Findings: The kinase RIPK4 functions as a tumor suppressor by restraining oncogenic $Kras^{G12D}$-driven skin tumor growth.

Research goal: To explore whether allosteric activators of RIPK4 can enhance its tumor-suppressive function, offering new therapeutic avenues for skin cancer.

Maelfait Team – Nucleic Acid Sensing in Cell Death and Inflammation

Focus: The role of nucleic acid sensors in antiviral defence and cellular stress responses.

Key findings: The sensor ZBP1 detects Z-shaped nucleic acids (RNA, DNA) and triggers apoptosis or necroptosis to limit viral dissemination or activate adaptive responses. When dysregulated, these pathways can drive interferon-mediated autoimmune diseases. Research questions: How are Z-shaped nucleic acids stabilized during viral

infection and stress? Do certain nucleic acid sequences favour Z-conformation? Which signalling pathways connect ZBP1 activation to cell death and inflammation?

Research goal: To provide molecular insights that pave the way for therapeutic targeting of ZBP1-driven autoinflammatory diseases.

Bertrand Team – Signal Transduction in Cell Death and Inflammation

Focus: Molecular mechanisms that regulate the interplay between cell death, cell survival and inflammation.

Key findings: The team identified several molecular brakes that prevent TNF-mediated cell death, including an unconventional form of autophagy that recognizes cytotoxic complexes and directs them to lysosomal degradation.

Research goal: To characterize and target these regulatory checkpoints, aiming to limit pathological inflammation in autoimmune and inflammatory diseases or to enhance (TNF-driven) killing of cancer cells.

Cell Death and Inflammation Unit – One unit, four interacting teams

The Cell Death and Inflammation Unit is part of the VIB-UGent Center for Inflammation Research (IRC) at Technology Park Zwijnaarde. It brings together four closely collaborating teams led by permanently appointed professors at Ghent University: Mathieu Bertrand, Wim Declercq, Jonathan Maelfait, and Peter Vandenabeele, head of the unit. The unit currently (2025) consists of four technicians, seven postdocs, one 10% visiting postdoc, one postdoc bioinformatician, and eight PhD students, organized into four teams. This collaborative structure enables strong interactions between research groups while maintaining complementary scientific expertise.



Peter Vandenabeele. © Cell Death and Inflammation Unit



Mathieu Bertrand. © Cell Death and Inflammation Unit



Jonathan Maelfait. © Cell Death and Inflammation Unit



Wim Declercq. © Cell Death and Inflammation Unit

Peter Vandenabeele obtained his PhD (1990) at Ghent University. In 1996, he became a Principal Investigator at the Flanders Institute for Biotechnology (VIB) and currently heads the Cell Death and Inflammation Unit.

Mathieu Bertrand obtained his PhD (2005) at University of Namur and carried out a postdoc at McGill University (2005–2009). He joined the unit in 2009 and became team leader of Signal Transduction in Cell Death and Inflammation. He was appointed Associate Professor at Ghent University in 2011 and Assistant Professor in 2016.

Jonathan Maelfait obtained his PhD (2011) at Ghent University, followed by a postdoc at Oxford University (2012–2017). He joined the unit in 2018 to lead the Nucleic Acid Immunity Team. In 2024, after securing an ERC Consolidator Grant, he was appointed Full Professor at Ghent University.

Wim Declercq obtained his PhD (1997) at Ghent University. He joined the unit at its foundation in 1996 to lead the Cell Death and Inflammation in the Skin Team. Since 2018, he has also served as Head of the Department of Biomedical Molecular Biology.

[Cell Death and Inflammation Unit]

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