DR. JOSEF STEINER KREBSFORSCHUNGSPREIS 2025

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Der 24. Dr. Josef Steiner Krebsforschungspreis
geht an Frau Dr. Anna Christina Obenauf.

Frau Dr. Obenauf ist Forschungsgruppenleiterin am Forschungsinstitut für Molekulare Pathologie der Universität Wien.

Die Preissumme beträgt gesamthaft CHF 1‘000‘000.

Dr. Josef Steiner Krebsforschungspreis 2025

Doktor Josef Steiner, Inhaber der „Dr. Steiner Apotheke und Bahnhofdrogerie“ in Biel, hat bei seinem Tode im Jahre 1983 ein grosses Vermögen hinterlassen, welches entsprechend seinem letzten Willen die finanzielle Basis der Dr. Josef Steiner Krebsstiftung bildet. Ziel der Stiftung ist die Förderung der Krebsforschung und die Auszeichnung hochverdienter Wissenschafter auf allen Gebieten der Krebsforschung. Als erster Preisträger konnte 1986 ein Schweizer, Dr. Peter Cerutti, geehrt werden. Seither konnten zahlreiche hervorragende Wissenschafterinnen und Wissenschafter aus Europa, USA, Australien und der Schweiz mit dem Dr. Josef Steiner Preis ausgezeichnet werden.

Im Bestreben, die Krebsforschung im Sinne des Stifters effizient und nachhaltig zu fördern, wurden 1998 die Richtlinien der Stiftung geändert. Anstelle eines persönlichen Preises wird seither ein hervorragendes Forschungsprojekt für die Periode von vier Jahren mit einem Betrag von 1’000’000 Schweizerfranken unterstützt. Der Forschungsgruppenleiter oder die Forschungsgruppenleiterin wird zusätzlich mit einem persönlichen Preis in der Höhe von 50'000 Schweizerfranken ausgezeichnet.

Die Auswahl des preisgekrönten Projektes erfolgt nach einem mehrstufigen, strengen Auswahlverfahren. Der Dr. Josef Steiner Preis 2025 wurde in renommierten Wissenschaftszeitschriften ausgeschrieben. Die eingereichten Projektskizzen wurden vom Stiftungsrat und einer aus Fachvertretern zusammengesetzten Preiskommission gesichtet und bewertet. Als Kriterien wurden die wissenschaftliche Qualität und die Originalität der Projektskizzen, die Qualifikation der Projektverfasser, sowie die Beurteilung der Machbarkeit der vorgeschlagenen Projekte in Betracht gezogen. Sechs hervorragende Projektskizzen wurden ausgewählt und die Verfasserinnen und Verfasser aufgefordert, ein überarbeitetes und detailliertes Projekt einzureichen. Für die Projekte wurden 2 vergleichende Beurteilungen von externen Gutachtern eingeholt.

Zusätzlich wurden die sechs Projektverfassenden zu einem Minisymposium am Institut für Physiologie eingeladen, welches Ende Januar 2025 im Beisein der Preiskommission und des Vorstandes der Stiftung stattfand. Anlässlich dieses Symposiums konnten die Forscherinnen und Forscher ihre Projekte vorstellen. Aus dem gesamten Auswahlverfahren ist Frau Dr. Obenauf als Gewinnerin hervorgegangen.

Laudatio für Frau Dr. Anna Christina Obenauf

Die Dr. Josef Steiner Stiftung verleiht den Josef Steiner Krebsforschungspreis an Dr. Anna Christina Obenauf in Anerkennung ihrer wegweisenden Forschung zu den molekularen Mechanismen der Therapieresistenz und der Umgehung der Immunantwort bei Krebserkrankungen*. Durch die Entwicklung innovativer experimenteller Modelle und mit Hilfe integrativer molekularer Analysen hat sie aufgedeckt, wie zielgerichtete Krebstherapien die Sekretion von Faktoren auslösen, welche das Überleben und die Ausbreitung resistenter Krebsklone fördern. Ihre Arbeit hat außerdem gezeigt, dass behandlungsresistente Tumore die körpereigene Immunantwort aktiv unterdrücken und so eine Kreuzresistenz gegenüber Immuntherapien aufbauen. Diese bahnbrechenden Entdeckungen tragen dazu bei, unser Verständnis der Tumoranpassung zu verbessern und eröffnen damit neue Wege zur Überwindung der Resistenz bei metastasierendem Krebs.*

Curriculum Vitae

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Present Position

2022- **Principal Investigator – Senior Group Leader, tenured**
Research Institute of Molecular Pathology (IMP), Vienna BioCenter, Vienna

Education

2002-2006 B.Sc./M.Sc. studies in Molecular Biology, Karl Franzens University of Graz, Austria

2007-2010 PhD studies, Department of Human Genetics, Medical University of Graz, Austria

Postdoctoral Career

2010-2015 Postdoctoral Research Associate, Memorial Sloan Kettering Cancer Center (MSKCC), New York, USA; Supervisor: Joan Massagué

2016-2022 Principal Investigator – Junior Group Leader, Research Institute of Molecular Pathology (IMP), Vienna BioCenter, Vienna, Austria

2022- Principal Investigator – Senior Group Leader with tenure, Research Institute of Molecular Pathology (IMP), Vienna BioCenter, Vienna, Austria

Awards and Fellowships

2024 ERC Consolidator Grant "*UnlockIT"*

2023 Election as full EMBO member

2023 Election to Scientific Editorial Board of Cancer Discovery

2022 Promotion to Senior Group Leader with tenure at the IMP

2022 AAAS Martin and Rose Wachtel Cancer Research Award

2021 Election to the EMBO Young Investigator Programme (YIP)

2019 Election to the Austrian Academy of Sciences (OeAW, Young Academy)

2017 ERC Starting Grant "*CombaTCancer"*

2015 ASCINA award (award for postdoctoral research)

2010 Erwin-Schroedinger postdoctoral fellowship, FWF, Austrian science fund

2010 Award of Excellence (award for outstanding PhD theses)

Grant Support *(active only)*

2024 – 2029 **ERC Consolidator Grant**, Single-PI Grant led by Anna Obenauf
Topic: Unlocking a T cell mediated immune response in therapy-challenged tumors "UnlockIT". Role: PI2024 – 2029

2024 – 2029 **FWF Excellence Program – Emerging Fields**
Topic: Devising Advanced TCR-TC to eradicate **OsteoSarcoma "Dart2OS"**. Role: Co-PI (6 groups)

2024 – 2027 **EU Horizon 2020 / Marie Skłodowska-Curie Actions Innovative Training Network** Topic: Deconstructing the adaptative evolution of metastasis "AdaptMET". Role: Co-PI (15 groups)

2024 – 2027 **Swiss Bridge Award**
Topic: Rational combination therapies to target persister cells "COMBAT-PERSIST". Role: PI

2022 – 2026 **Alex's Lemonade stand Crazy 8**
Topic: Understanding and inhibiting mechanisms of metastatic spread in **osteosarcoma**, Role: Co-PI (5 groups)

Most significant publications

1. Elewaut A*, Estivill G*, Bayerl f, Hoffmann-Haas L, Novatchkova M, Nguyen TV, Andreatta F, Vulin M, Pottendorfer E, Krecioch I, Holstein F, Cronin SM, Rieser S, Muñoz i Ordoño M, Wiesner W, Zuber J, Böttcher JP, Vanharanta S, **Obenauf AC#.** Cancer cells impair monocyte-mediated intratumoral T cell stimulation to evade immunity. **Nature.** 2024 Nov 27. doi: 10.1038/s41586-024-08257-4.
2. Leiendecker L, Neumann T, Jung PS, Cronin SM, Steinacker TL, Schleiffer A, Schutzbier M, Mechtler K, Kervarrec T, Laurent E, Bachiri K, Coyaud E, Murali R, Busam KJ, Itzinger-Monshi B, Kirnbauer R, Cerroni L, Calonje E, Rütten A, Stubenrauch A, Griewank KG, Wiesner T#, **Obenauf AC#.** Human papillomavirus 42 drives digital papillary adenocarcinoma and elicits a germ-cell like program conserved in HPV-positive cancers. **Cancer Discovery**. 2022 Oct 10:CD-22-0489. doi: 10.1158/2159-8290.CD-22-0489.
3. Haas L, Elewaut A, Gerard CL, Umkehrer C, Pedersen M, Leiendecker L, Krecioch I, Hoffmann D, Novatchkova M, Kuttke M, Neumann T, Pires de Silva I, Witthock H, Cuendet MA, Carotta S, Harrington KJ, Zuber J, Scolyer RA, Long GV, Wilmott JS, Michielin O, Vanharanta S, Wiesner T, **Obenauf AC#**. Acquired resistance to targeted therapy confers cross-resistance to immunotherapy. **Nature Cancer.** 2021 2, 693–708. doi: 10.1038/s43018-021-00221-9.
4. Leiendecker L*, Jung PS*, Neumann T, Schleiffer A, Mechtler K, Wiesner T*, **Obenauf AC*#**. LSD1 inhibitors induce neuronal differentiation of Merkel cell carcinoma by disrupting the LSD1-CoREST complex and activating TGFb signalling. BioRxiv (2020.04.14.041657), **EMBO Mol Med.** 2020 Nov 6;12(11):e12525. doi: 10.15252/emmm.202012525.
5. Umkehrer C, Holstein F, Formenti L, Jude J, Froussios K, Neumann T, Cronin SM, Haas L, Lipp JJ, Burkard TR, Fellner M, Wiesner T, Zuber J, **Obenauf AC#**. CaTCH - A barcode-guided CRISPRa-inducible reporter to isolate clones from heterogeneous populations. **Nature Biotechnology**. 2020 Jul 27. doi: 10.1038/s41587-020-0614-0.
6. **Obenauf AC**, Ji AL, Zou YZ, Vanharanta S, Shu W, Shi H, Kong X, Bosenberg MC, Wiesner T, Rosen N, Lo RS, Massague J. Therapy induced tumor secretomes promote resistance and cancer progression. **Nature.** 2015 Apr 16;520(7547):368-72. doi: 10.1038/nature14336.
7. Wiesner T, Lee W, **Obenauf AC**, Ran L, Cao Z, Murali R, Sboner A, Landa-Lopez I, Button J, Shukla S, Gao D, Shah R, Scott SN, Wang L, Merghoub T, Ladanyi M, Schwartz G, Fagin JA, Busam KJ, Berger MF, Chen Y, Chi P. A novel ALK isoform arises through de novo alternative transcriptional initiation and drives oncogenesis. **Nature.** 2015 Oct 15;526(7573):453-7. doi: 10.1038/nature15258.
8. Valiente M, **Obenauf AC**, Jin X, Chen Q, Zhang XH, Lee DJ, Chaft JE, Kris MG, Huse JT, Brogi E, Massagué J. Serpins promote cancer cell survival and vascular co-option in brain metastasis. **Cell**. 2014 Feb 27;156(5):1002-16. doi: 10.1016/j.cell.2014.01.040.
9. Massague J, **Obenauf AC**. Metastatic colonization by circulating tumor cells. **Nature**. 2016 Jan 21;529:298–306. doi: 10.1038/nature14336.

*contributed equally, #corresponding author, members of the lab underlined

A full list of publications (46 peer reviewed papers including 8 reviews) is available at:
https://pubmed.ncbi.nlm.nih.gov/?term=obenauf+a&sort=date

Dr. Obenauf beschreibt ihr preisgekröntes Projekt wie folgt:

Decode-iTME:
Unlocking the Immune System's Full Potential Against Cancer

Immunotherapies—treatments that empower the body's own immune system, especially T cells, to recognize and destroy cancer—have revolutionized modern oncology (Pardoll, 2012; Topalian et al., 2012). These approaches were made possible by groundbreaking discoveries that recently earned a Nobel Prize, and they have led to remarkable, life-saving outcomes for many patients. Yet, despite these advances, immunotherapies are not a universal cure. In too many cases, they fail to produce lasting responses (Obenauf, 2022). Some tumors initially shrink, only to return months later—stronger, more aggressive, and more resistant than ever. Others don't respond at all, leaving patients and physicians with limited treatment options.

Why do these powerful treatments work so well in some people but not in others?

The answer lies not just in cancer cells themselves, but in a dynamic and complex ecosystem that surrounds these cells, the tumor microenvironment (TME) (Massagué and Obenauf, 2016; de Visser and Joyce, 2023). This network of immune cells, blood vessels, signaling molecules, and support structures can either support or suppress an immune attack. In many cases, tumors actively rewire the TME into a hostile zone that disables immune cells, which is called an immune-evasive tumor microenvironment, or iTME. In an iTME, even the most powerful T cells that could in principle recognize and kill the tumor cells, fail to penetrate the tumor or lose their killing capacity once inside (Joyce and Fearon, 2015; Binnewies et al., 2018). When this happens, even the most advanced immunotherapies struggle to make an impact.

The Decode-iTME project aims at unraveling this fortress around the tumor cells by understanding how it is built and by searching for new ways to dismantle it. The ultimate goal consists of reprogramming the iTME such that it not only lets immune cells in but helps them thrive and destroy tumors from within.

Resistance that spreads

One of the breakthrough findings of my team that forms the basis for this project, came from studying melanoma—an aggressive skin cancer that has served as a testbed for many modern therapies (Obenauf et al., 2015; Haas et al., 2018). In this study, we discovered something unexpected: when tumors develop resistance to a class of targeted drugs called RAF/MEK inhibitors (which block specific growth pathways in the cancer cells), they simultaneously become resistant to immunotherapies that are supposed to reinvigorate the immune system (Haas et al., 2021). This finding was surprising because these therapies target two entirely different aspects of the tumor thereby highlighting the existence of a strong cross-talk between the tumor and the immune system (Hugo et al., 2015).

This cross-resistance is deeply concerning because it limits treatment options. We found that resistant tumor cells actively secrete immune-suppressing molecules like PGE2, while dampening the production of immune-activating signals such as interferon-I (IFN-I) (Elewaut et al., 2025). This imbalance changes the behavior of nearby immune cells and dampens their potential to eradicate tumor cells.

Rewiring the immune ecosystem

Despite the grim picture painted by immune-evasive tumors, there is hope. We found that the immune-suppressive state of these tumors is not set in stone. By restoring the production of interferon or blocking PGE2 signals, tumors that were previously resistant once again become vulnerable to T cells (Zelenay et al., 2015; Bayerl et al., 2023; Elewaut et al., 2025). Even more exciting was the discovery of a new player in the immune response: activated monocytes and macrophages (Elewaut et al., 2025). These immune cells are more abundant than the dendritic cells traditionally thought to be the main players for restimulating T cells in lymph nodes and, as found recently, also inside tumors. These activated myeloid cells form so-called inflammatory hubs—tiny immune hotspots where they engage T cells, boost their activity, and equip them for the battle. In therapy-sensitive tumors, these hubs are plentiful. But in resistant tumors, they vanish. By understanding what causes this shift, Decode-iTME aims to bring these hubs back. If successful, this could mean that even deeply immune-evasive tumors can be turned into fertile ground for a renewed immune response.

Programming a smarter immune response

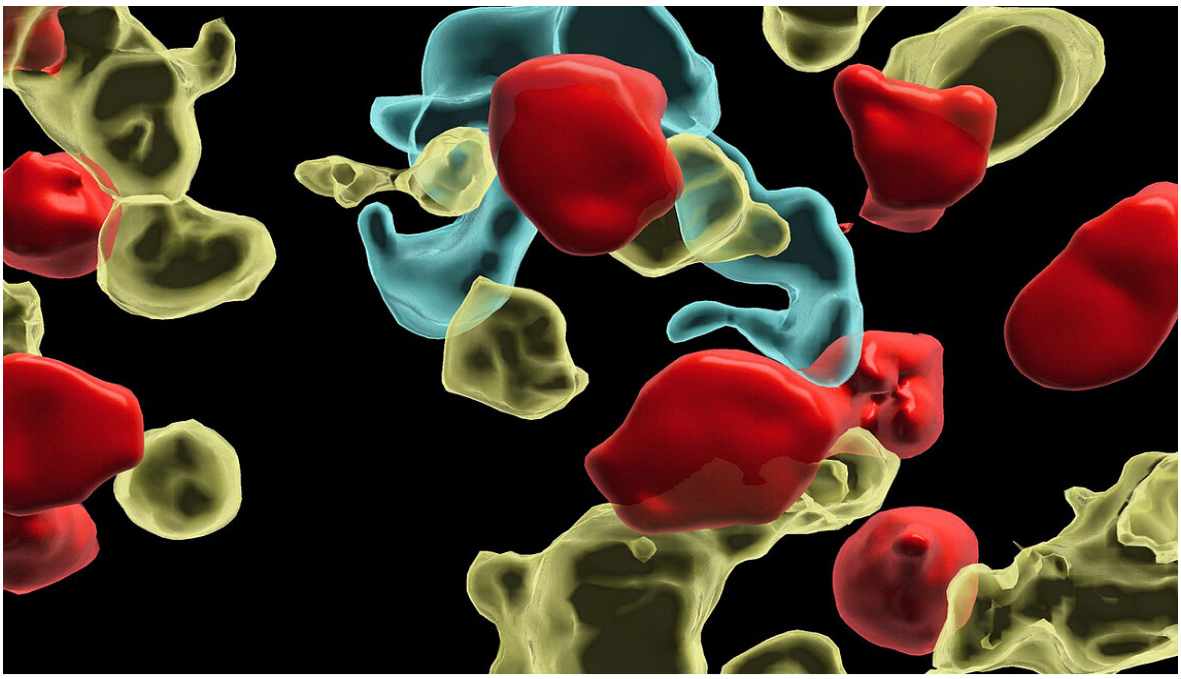
What if immune cells could be trained to detect an immune-evasive environment and respond accordingly? That's the vision behind the synthetic biology component of Decode-iTME. Using AI-powered tools pioneered by my colleague Alexander Stark (de Almeida et al., 2024), our team is designing 'smart switches' that can sense specific conditions within the tumor. These switches act like fire alarms: they remain silent in normal tissues but activate in the presence of an iTME. Once triggered, they instruct immune cells to release powerful therapeutic molecules such as interferon or other immune-activating cytokines, right where they are needed. This strategy should minimize harmful side effects because the therapy only activates in the tumor's immune-evasive environment. This precision approach represents a new frontier in immunotherapy—one where immune cells don't just attack, but are engineered to respond to their environment.

From discovery to patient impact

While Decode-iTME is rooted in cutting-edge basic science, its impact is designed to reach patients. The project focuses on melanoma, pancreatic cancer and lung cancer—cancers where therapy resistance and immune evasion are major hurdles. By working with real patient data and state-of-the-art lab models, we are ensuring that our findings translate from the bench to the bedside.

A new era of cancer immunotherapy

Decode-iTME represents a powerful convergence of cancer biology, immunology, and synthetic biology. With generous support from the Steiner Research Foundation, this interdisciplinary project is poised to advance our understanding of the mechanisms underlying immune resistance. Building on a strong foundation of data, cutting-edge tools, and talent, Decode-iTME has the strong potential to unlock new therapeutic pathways that could benefit cancer patients worldwide. I am deeply grateful for the Steiner Research Foundation's support and truly excited to launch this ambitious project.



Computer-rendered immunofluorescence image showing T cells (red) interacting with monocytes (yellow) and dendritic cells (blue) in the tumor microenvironment of a mouse melanoma tumor. These interactions help T cells to fully mature and effectively target and kill cancer cells. In an immune-evasive tumor microenvironment, these interactions are frequently impaired in which case T cells fail to kill cancer cells effectively.
Image credit: Anna Obenauf/IMP, Jan Boettcher/TUM.

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