# AMBITION STATEMENT ROADMAP FOR THE IMMUNOLOGICAL RESEARCH FIELD IN THE NETHERLANDS: VISION 2.0

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Advice from the Dutch Society for Immunology (NVVI)

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# Foreword

Before you lies the ambition statement *Roadmap for Immunological Research in the Netherlands*.

The importance of the immune system in health and disease is underscored by the fact that more than 25% of all candidate drugs currently being tested in clinical trials target the immune system. These include agents aimed at strengthening and/or training the immune response (such as in vaccination and cancer therapy) as well as agents that suppress immune system activity (such as for allergy and autoimmune diseases). The development of many new treatments depends on excellent fundamental and applied immunological research. A detailed understanding of the immune system is crucial for the development of safe vaccination strategies, innovative cancer immunotherapies, improved organ transplantation methods, and insight into abnormalities in the immune response, such as in allergy, autoimmune diseases, and blood cancers.

Over the past year, the Dutch Society for Immunology (NVVI) has worked on developing a vision for innovation in the immunological research field, for which we mapped the possibilities and barriers related to research involving minimal use of research animals.

To gain insight into the mechanisms underlying health in humans and animals (both in the wild and in livestock), immunology as an international discipline uses a rich diversity of both animal models and animal-free models. In the latter, immunological processes and the effectiveness and safety of substances such as vaccines are studied without using research animals. There are various types of animal-free models, and terms such as New Approach Methodologies (NAM), human measurement models, in silico models, and *in vitro* models each refer to different aspects of these alternatives. For clarity, we use the term animal-free methods as an umbrella term in this document.

The use of animals in experiments is strictly regulated in the Netherlands and the EU. There is more legislation and regulatory oversight for research animals than for any other kept animal species. Requirements are imposed on the qualifications of personnel caring for the animals, the housing systems used, and the experiments performed with animals. If the intended research goals can reasonably be achieved without animal experimentation, then it is prohibited to conduct animal experiments for these goals.

Dutch immunological research holds a leading international position. This is thanks in part to the essential combination of *in vivo* research in animal models and *in vitro* research using animal-free models, which has demonstrably led to the development of new medicines and diagnostics for both humans and animals. Within immunology, there is a strong intrinsic motivation to use the most appropriate research models necessary to answer the scientific questions at hand. These may include animal-free methods, animal models, or a combination of both. Immunologists actively contribute to the innovation of both animal-reducing and animal-free methods. Examples include advanced flow cytometry (FACS) of immune cells in blood and organs, innovative cell and tissue culture technologies such as organoids and organ-on-a-chip models, new imaging techniques, and genome-wide analyses at single-cell level (single-cell sequencing and *in situ* transcriptomics).

For many immunological questions related to health and disease, no suitable alternative to an animal model currently exists. This is understandable, as immune responses or immunological disorders typically involve numerous organs: the affected organ (e.g., the intestine in Crohn's disease or the lungs in respiratory infections), draining lymph nodes, the bloodstream, spleen, brain, and immune cell production organs like the bone marrow and thymus. Modeling this complexity, including many compartments and migratory cell types, using organoids or organs-on-a-chip is a Herculean task. While new developments such as multi-organ-on-a-chip systems and complex organoids provide valuable insights and opportunities, these models still only partially reflect the complex biology of the immune system.

The ambition of the NVVI is to consolidate and strengthen the prominent position of Dutch immunology, both in human and veterinary fields, so it can continue to contribute optimally to improved health, prevention, and therapies. At the base of this ambition is the scientifically optimal choice of the best models to answer relevant research questions. This includes a strategic and rational combination of (disease) models both with and without the use of animals.

For better science whilst using fewer animal models it is essential to continue developing new immunological measurement models that are more representative and predictive for patients than animal models. Given the exceptional complexity of the immune system and its involvement of many organs, we face significant challenges in this endeavor. It will not be feasible in the short term to develop effective animal-free models for every disease condition.

To make the most of internationally recognized top-tier immunological research in the Netherlands and to keep developing medicines and therapies, we cannot yet fully do without animal models. We therefore advise investing in further innovation of scientifically sound research models that provide reliable new insights. Where possible, these should be animal-free methods, but they may also include innovative animal research models aligned with the 3Rs principle (refinement, reduction, replacement). Figure 1 of the consensus document illustrates the current landscape of available models for studying the immune system.

On November 11, 2024, the Royal Netherlands Academy of Arts and Sciences (KNAW) organized a symposium in which participants discussed the advantages and disadvantages of innovative technologies, for animal-free models as well as animal models. Immunologists contributed as organizers and panelists, and the audience included crucial input from amongst others patient organizations, clinical immunologists, and oncologists. One of the conclusions was that despite all positive developments in animal-free methods, widely supported by all, immunological research cannot yet be conducted without the use of animals. During this symposium the concept of *animal-wise research* was proposed which includes both animal-free approaches and the carefully justified use of minimal numbers of research animals.

In the next five years, NVVI aims to make significant progress in both developing animal-free immunological measurement methods and advancing the refinement and reduction of animal models. Due to the immune system's high complexity, it is not currently possible to set a realistic timeline for fully phasing out animal models in immunological research without compromising quality and usefulness.
The goal of this ambition statement is to keep the discussion about selecting the most appropriate models for scientific questions alive and to remain in dialogue with researchers on this matter. To that end, we have formulated seven recommendations.

## Creation of this Document

To develop a widely supported roadmap within the immunological research field, we launched a series of initiatives between December 2023 and December 2024. These included the formation of a sounding board group, input from yNVVI, and a consultation open to all 1,200 NVVI members. This consultation took place both in writing and verbally during a feedback session at the annual meeting on December 11–12, 2024. Additionally, a draft version of this document was made available to all NVVI members via the NVVI website.

# Unique Aspects of Immunology in Relation to Animal and Non-Animal Models

- Immunology is an extremely dynamic field, responsible for numerous Nobel Prizes and Lasker Awards (see table in the appendix). Animal models, for instance, were essential in the early development of cancer immunotherapy and mRNA vaccines, including those for COVID-19.
- These breakthroughs have had many direct and indirect impacts, which are difficult to overstate, on the health of both humans and animals
- Within the immunology field, there is significant attention for the development and application of new measurement methods and technologies aimed at reducing or avoiding the use of research animals. The immune system not only plays a vital role in defense but also during physiological development and processes such as tissue repair, metabolism, thermoregulation, and behavior in both animals and humans. It is composed of a diverse array of mechanisms that provides protection and repair in virtually every conceivable anatomical compartment. Due to this complexity, the immune system presents a challenge to be modelled reliably and comprehensively using only immunological measurement models fully outside of intact living organisms. Nevertheless, continued development and validation of animal-free models will further reduce the use of research animals.
- In the Netherlands, immunology primarily focuses on fundamental and translational scientific research, and to a lesser extent on (legally required) safety testing.

# Roadmap for the Immunological Research Field in the Netherlands: Vision 2.0

Immunology focuses on understanding the processes underlying the pathologies of infectious and immune-related diseases in both humans and animals. This knowledge is essential for developing interventions to treat or prevent such diseases. Both fundamental and applied immunological research form the foundation for understanding these processes. The immunological knowledge gained is often also crucial for other research areas such as cancer, cardiovascular diseases, and metabolic and neurological disorders.

Research using animal models forms the basis of our knowledge and understanding of the immune system and the treatment and prevention of many diseases. This is underscored by the contribution of animal models to groundbreaking immunological discoveries, which have led to over 110 Nobel and Lasker Prizes. The immune system functions within a complex network of interrelated processes. Although animal models do not reflect all aspects of human immunology and disease, they currently still remain essential to the immunology field and to our knowledge, understanding and treatment of diseases in which the immune system plays an important role.

Immunological research is evolving rapidly, and new technological and medical advances have led to the development of novel immunological measurement models. Depending on the scientific question, these can complement or potentially partially replace animal models. These animal-free methodologies allow for detailed investigation of specific immunological processes without involving animal models. Despite rapid developments, these methodologies also have limitations, and many still require validation. High-quality scientific research is characterized using innovative measurement methods that are best suited to answer the specific research questions. For immunological research, this means using animal models only when the research question cannot be answered by other means.

The immune system functions as a complex interplay of numerous interacting processes. Therefore, it is reasonable to assume that in addition to the development of animal-free methods, animal models will continue to play an important role for the time being. This Ambition Statement or Roadmap 2.0 aims to present a realistic view of the use of animal models in immunology and the potential replacement thereof by animal-free methods. Where possible, recommendations are made for the development, improvement, and implementation of animal-free methodologies. The possibility of fully replacing animal models with animal-free methods in the short or medium term is, at this time, not realistic.

We want to emphasize that a proefdierwijze (animal-wise) approach—encompassing both animal-free research and the careful, minimal, use of animals—should be central to addressing scientific questions. Once a research question has been carefully formulated, it should first be examined whether it can be answered using only animal-free methods. Only if that is not possible should the necessary animal experiments be determined in a way that minimizes animal distress and the number of animals used. This is guided by the 2Rs of Reduction and Refinement.

Although this roadmap focuses primarily on human immunology, there is also important immunological research aimed at animal health. This involves not only farm and companion animals, but also for example, wild birds, as avian influenza affects both domesticated poultry and wild birds, and by now also several other species. The COVID-19 pandemic has strongly highlighted the shared interest of animal and human health (One Health concept), particularly the risk of zoonotic pathogens, those that can jump from animals to humans. In such cases, a combination of animal models and animal-free models is essential to safeguard the health of both humans and animals. In many cases, the target animal species itself is used as the model to improve its health.

The following seven recommendations are proposed:

## 1. Ensure Clear Communication and Set Realistic Expectations: Towards Researchers, the Public, Policymakers, and Patients. Involve All Stakeholders.

Within the field of immunological research, experimental knowledge is generally shared through scientific publications and during conferences. However, this mode of communication does not reach the wider audience (broader public) or political sphere. To clarify why research using research animals is still conducted and simultaneously demonstrate that efforts are underway to develop more refined animal models and alternative animal-free immunological measurement models, broad and transparent communication from the immunological research community is essential. This communication must be aimed at the public, patients, and policymakers, offering a realistic portrayal of both the possibilities and limitations of animal-based models as well as animal-free alternatives. The dialogue should begin with the following basic question: What do we, as immunologists, aim to achieve with our research?

We acknowledge that conservatism toward animal-free innovation exists and must be addressed. To enable a true transition toward the replacement of animal models, where possible, it is critical how, and by whom, the message is communicated, both to fellow researchers and to society at large. Creating a realistic perspective on the possibilities and limitations of animal-free methods, as well as the continued use of animal models, is essential in this context.

One notable development in this area is the Transparency Agreement on Animal Research, which has been signed by many Dutch universities, academic hospitals, and research institutions, many of which also conduct immunological research on humans and animals. The goal of this agreement is to provide society with optimal openness regarding animal research, the development of new animal-free immunological methods, the research being conducted, and why it benefits human and animal health. Publishing balanced examples of impactful developments in accessible media for the public can play an important role in this effort.

It is important that the NVVI remains in dialogue with organizations such as Transitie Proefdiervrije Innovatie (TPI), Stichting Proefdiervrij, and the Center for Animal-Free Biomedical Translation to allow for open discussions and the sharing of perspectives. Joint communication about what is and is not yet feasible in immunological research can help reduce polarization (see for example: Homberg et al., Frontiers in Veterinary Science, doi: 10.3389/fvets.2024.1303744). In addition, it is also crucial that patients and patient organizations are involved in these discussions.

The immunological research community is committed to phasing out the use of research animals over time, without compromising the quality and utility of the research. However, due to the complexity of the immune system and the nature of immunological research, setting a definitive timeline would create unrealistic expectations and is therefore not currently feasible.

## 2. Consider Revising the Terminology ‘Animal-Free Models’

It is crucial that all stakeholders are involved in the transition toward the replacement of animal usage in immunological research. This means ensuring that everyone involved trusts that the discussion is not being conducted selectively but is genuinely inclusive. Previous communication efforts and discussions surrounding the reduction or replacement of animal research (e.g., ‘The Netherlands as a World Leader in Animal-Free Innovation by 2025’) have, in fact, contributed to the polarization of the debate—pitting stakeholders against each other rather than encouraging collaboration. To promote inclusivity and objectivity, terminology in the debate must be chosen carefully.

Using terms such as transition and animal-free may create the impression among stakeholders that the move toward animal-free methods is already a foregone conclusion, regardless of whether sufficient scientific justification has been provided. Alternative terms like immunological measurement models or human-based models, instead of animal-free models, shift the focus to what we aim to achieve, rather than what we seek to exclude. This requires clear and careful communication, with a well-defined, shared goal, as further outlined in Recommendation 3 below.

There are various approaches to conducting research without the use of research animals. Depending on the technique, different terms are used, such as New Approach Methodologies (NAM), human-based models, in silico models, and *in vitro* models, each referring to specific aspects of these methods. While we propose using a different term, for the sake of readability, this document will continue to use the umbrella terms 'animal-free methods' and 'animal-free models'.

## 3. Initiate the Dialogue from a Shared, Broadly Supported Ambition: Striving for Excellent Science With Less or No Use of Animal Models

The ambition to innovate immunological research is supported by many stakeholders. Within the framework of animal-wise science, animal experiments have long been used to gain new insights and develop treatments. There is ongoing awareness of the limitations and ethical implications associated with the usage of animal models and there is a growing desire to find alternatives.

The use of animals in scientific research is a complex and often emotionally charged subject. Balancing ethical concerns with scientific progress is essential and is at the heart of both the EU Directive and the Dutch Animal Experiments Act.

At present, there are no animal-free models capable of fully capturing the complexity of immune responses, nor of completely replacing the need for animal models. It is not currently possible to make a realistic prediction about when that situation might change. At the same time, we emphasize that animal models also have their shortcomings and do not always represent human biology accurately. The guiding principle of the NVVI is to conduct top-tier immunological research that benefits human and animal health using as few animals as possible, or none at all. This must be the basis of the ongoing dialogue.
To prevent polarization in the discussion surrounding animal use and to achieve the shared goal of animal-wise innovation, an open and transparent dialogue is needed between scientists, clinicians, industry, animal welfare organizations, governments, societal groups, and patient organizations. It is important to emphasize that efforts to reduce or phase out animal use must never come at the cost of our ability to gain meaningful insights into the development and treatment of infectious diseases, allergies, autoimmune conditions, chronic inflammation, and cancer. In short: Excellent science with, where possible, less or no use of research animals.

It must also be recognized that animal experiments are often essential for validating the safety and effectiveness of animal-free methods. Therefore, the conversation must allow room for nuance and be built around an integrated approach that takes into account all aspects of both animal use and animal-wise innovation.

To develop a shared Immunology Roadmap toward the reduction and eventual phase-out of animal use in research, investments must be made in innovative technologies and methodologies. This includes adequate funding and time for both the development of animal-free methods, such as *in vitro* models (cultures, organoids, organ-on-a-chip, etc.), computer modeling, and clinical studies in volunteers, as well as for innovative animal models that embody the principles of refinement and reduction. An example includes integrating natural commensals and pathogens into animal models (see also Rehermann et al., Nat Rev Immunol, 2025, doi: 10.1038/s41577-024-01108-3).

It is also important to raise awareness among researchers and within training programs about the possibilities of these animal-wise innovations. The NVVI plays a central role in this effort: during its annual two-day Spring Meeting (200–300 participants), attention must be devoted to this topic, as well as during the two-day Winter Meeting (500–600 participants). On a European level, through the European Federation of Immunological Societies, the NVVI should also seize opportunities to advance the dialogue on animal-wise innovation.

In summary, the pursuit of animal-wise innovation in immunological research is an ambitious goal that requires collaboration and awareness of both the challenges and opportunities. The NVVI considers it one of its key priorities to facilitate this dialogue and to work alongside all stakeholders toward a better future, for patients and research animals alike.

## 4. Make Optimal Use of Existing Expertise in Disease Model Development

In the context of the transition to animal-wise innovation in immunological research, it is essential to have a clear overview of currently available animal and non-animal models, along with the corresponding expertise. Because immunology plays a key role across multiple scientific domains, it is important to involve researchers from related fields as well.

Within the Dutch immunology field, numerous initiatives are underway involving the development and use of animal-free models for both human and animal health. The Netherlands holds a leading international position in this area.

Figure 1 provides an overview of different measurement models used in immunology. Examples of innovations in animal models include: the usage of invertebrate species such as fruit flies and C. elegans worms; the implementation of humanized mouse models; and training the mouse immune system with gut microbiota from wild mice, whereby its translationability to humans significantly increases.

For many immunological diseases (e.g., infection, inflammation, allergy, cancer) in both humans and animals, no adequate alternative to animal models currently exists. Sharing knowledge between research groups working with animal models and those focused on non-animal models can accelerate the deployment and development of new immunological/human-based measurement models or refined animal models.

Programs such as NWO's "More Knowledge with Fewer Animals" are valuable in this regard, enabling, for example, the funding of systematic reviews of existing literature on animal-based immunological research. These reviews help consolidate knowledge on animal models and potentially suitable animal-free immunological methods, which can then be more widely disseminated through publications.

It's also essential to consider that reagents used in human-based models often contain animal-derived components or are produced using animal-based systems, which should not be overlooked. The broad application of Open Science principles is therefore highly important. Other key resources include the Dutch consortium Human Disease Models and Technologies (hdmt.technology), the 3Rs Centre Utrecht (Utrecht University), and the UK-based NC3Rs (nc3rs.org.uk), all of which offer extensive examples and databases.

Refinement in animal research also involves enhancing the translational value of existing animal models. Recent developments show that, for instance, refinement through semi-naturalistic housing and enrichment leads to improved models with healthier animals, and thereby more translatable results to humans.

It is essential for both patient and animal welfare that funding for human-based models keeps pace with funding for the refinement and improvement of animal models.

## 5. Continue Providing Financial Support for the Development and Validation of Animal-Wise Measurement Models

Various promising animal-free models have been developed to study specific aspects of the immune system. The availability of new financial resources—such as those from the National Growth Fund and the establishment of the Center for Animal-Free Biomedical Translation (Utrecht)—will accelerate these developments. Validation and standardization of these measurement models are crucial, enabling reproducibility across different laboratories.

A current challenge is securing sufficient funding specifically for the validation and standardization of these models. It's important to also consider the needs of industry, facilitating a complementary collaboration between academia and business. Early engagement with regulatory bodies (e.g., the EMA) is also vital.

When developing animal-free methods, attention must be paid to their eventual use in drug approval and therapeutic applications. This avoids creating models that are too complex, insufficiently reproducible, or prohibitively expensive, leading to poor adoption due to unreliable outcomes. Key obstacles to overcome include unclear validation processes, misaligned expectations between researchers and end-users, and lengthy validation timelines. These introduce risks that hinder further development or uptake. Since both animal models and animal-free innovations only mimic part of the biological complexity, involving end users in the validation process is essential. Their input ensures that the innovation meets user needs and is applicable to specific research questions.

One solution is to provide additional funding specifically for validating existing non-animal models, alongside investments in new innovations. Ideally, this should be done in collaboration with industry, and regulatory authorities should be involved early to streamline the acceptance process. Validated models will more likely be adopted by companies and institutions, reducing animal usage for similar research purposes.

Importantly, alongside financial support for animal-free models, it is important that also financial support is (continued to be) made available for the refinement and enhancement of animal models, alongside animal-free models.

## 6. Integrate the Development of Animal-free Models into Legislation and Policy

Although legally mandated toxicity and safety studies fall outside the direct focus of the NVVI and Dutch academic immunology, they are still relevant to this roadmap. Until recently, all drugs were required to undergo animal testing for toxicity. Recent changes now allow for non-animal test methods to replace animal studies, provided they are validated and proven reliable. This is a major regulatory shift that could reduce animal usage in legally required studies.

Achieving this shift won't happen overnight. Many non-animal measurement methods are still in development and must undergo rigorous validation before gaining regulatory acceptance.
Revising international legislation and guidelines could bring about a paradigm shift, making animal research for legally mandated testing no longer the default. This will require strong collaboration between researchers, regulatory bodies, and governments. It is worth noting, however, that legally mandated testing only accounts for a portion of all animal experiments.

## 7. Promote Education on a Wide Range of Immunological Models, Both Animal and Non-Animal based, For Young Researchers

To raise broader awareness and knowledge within the scientific community about (new) animal and animal-free immunological measurement models, education must be developed and continuously kept up to date.

Early exposure to model systems is crucial. Academic programs, such as Biomedical and (Bio)Pharmaceutical Sciences, should devote specific attention to innovative models like 3D cell cultures, organoids, and organs-on-a-chip, as well as refined animal models for studying disease processes and therapeutic modalities. While this is already happening at some universities, this can be expanded further.

For early-career researchers, such as PhD candidates, the NVVI can organize course days and symposia dedicated to a broad range of innovative research models in immunology. A current example of where this already happens is the Netherlands Respiratory Society's annual Advanced Technology in Lung Research symposium. These events should address both refined animal models and innovative non-animal models. It is important to emphasize that model selection depends on the research question and translational value to humans or target species.

Next to early-career researchers, established researchers should also be kept informed about these developments through webinars, conferences, and publications, which help disseminate knowledge internationally and underscore the global leadership of Dutch immunology in animal-wise innovation. To implement this structurally, universities and research institutes, with support from government funding, must commit to developing comprehensive education programs.

By empowering researchers to identify and use the most suitable models, the use of non-animal alternatives will naturally increase where possible. This will result in reduced animal use, safeguard the world-class standing of Dutch immunological research, and further establish the Netherlands as frontrunner in positioning in animal-wise innovation.

# Summary

## Ambition Statement – Vision for Immunology 2.0


- Following an open call by the NVVI, this Vision for Immunology 2.0 was developed with input from immunologists across various disciplines and at different stages of their careers. Contributions were provided through online meetings, written feedback, and an open consultation session during the NVVI Winter Meeting in December 2024.
- A draft version of Vision 2.0, which includes seven detailed recommendations, was made available to all NVVI members via the website, with the opportunity to provide feedback.
- In writing Vision 2.0, key elements from the original Vision for Immunology were incorporated and built upon.
- The NVVI board supports robust scientific initiatives aligned with the 3Rs principles (Refinement, Reduction, Replacement), for human-based measurement models as well as for animal models, which both remain indispensable for the foreseeable future
- Dutch immunology is internationally renowned and plays a leading role in the development of new drugs and therapies. The NVVI aims to consolidate and expand this position. To achieve this, it is vital that immunologists have access to the best possible approaches and technologies, enabling them to deliver the greatest scientific value for both humans and animals. The scientific question must always be the starting point, guiding the selection of the most appropriate research model—within the framework of harmonized European legislation, which provides an adequate ethical foundation.
- Many successful research groups in immunology and immuno-oncology combine animal models with human-based measurement models. This integrated approach demonstrably leads to improved treatments, effective vaccines, and the development of new medicines, including immunotherapies for cancer, allergies, and autoimmune diseases.
- The Vision for Immunology 2.0 is aligned with the comprehensive Vision for Cardiovascular (Animal-Free) Innovation, and the supporting consensus article by Van der Velden et al. (Cardiovascular Research, 2022, https://doi.org/10.1093/cvr/cvab370).

# Appendix

| Models to study the immune system in health and immune disease | Animal models | Human | Human *In vitro* |
|---|---|---|---|
| Cellulair (pathological) mechanisms) | ☑ | ☑ | ☑ |
| Drug studies (toxicity and effectivity) | ☑ | ☑ | ☑ |
| Organ-organ interactions | ☑ | ☐ | ☐ |
| Cell-cell interactions | ☑ | ☑ | ☑ |
| Kinetics and initiation of immune pathology | ☑ | ☐ | ☐ |
| Organ-specific immune biology | ☑ | ☐ | ☑ |
| Behaviour | ☑ | ☐ | ☐ |
| *In vivo* imaging | ☑ | ☑ | ☑ |
| Genome-wide (single) immune cell characterization | ☑ | ☑ | ☑ |

| Tools to refine and reduce animal use | Animal models | Human | Human *In vitro* |
|---|---|---|---|
| High throughput analysis | ☑ | ☐ | ☑ |
| Genome editing | ☑ | ☐ | ☑ |
| *Ex vivo* human tissue studies | ☐ | ☑ | ☐ |
| Biobanking | ☑ | ☑ | ☑ |
| Data and registries | ☑ | ☑ | ☑ |
| Preclincial trials | ☑ | ☐ | ☐ |
| Computational modeling AI | ☑ | ☑ | ☑ |
| Sequential *in vivo* imaging | ☑ | ☑ | ☐ |

Fig. 1. Available models for immunological analyses (adjusted to Van der Velde et al, doi.org/10.1093/cvr/cvab370)

Table 1. Nobel prizes awarded for physiology or medicine, in the field of immunology

| Laureates *) | Year | Research title | Animals used |
|---|---|---|---|
| Emil von Behring | 1901 | Serum therapy, especially in its application against diphtheria | Cow, guinea pig, horse, rabbit, rat |
| Robert Koch | 1905 | Transmission and treatment of tuberculosis | Guinea pig, mouse, rat |
| Ilya Mechnikov, Paul Ehrlich | 1908 | Immunity in infectious disease | Guinea pig, mouse, birds, primates |
| Alexander Fleming, Ernst Chain, Howard W Florey | 1945 | Discovery of penicillin | Mouse |
| Max Theiler | 1951 | Yellow fever vaccine | Chicken, mouse, primates |
| Frank M Burnet, Peter Medawar | *1960* | Acquired immunological tolerance | Cow, mouse |
| Baruj Benacerraf, Jean Dausset, George D Snell | 1980 | Histocompatibility antigens and their mechanism of action | Guinea pig, mouse |
| Niels Jerne, George JF Köhler, Cesar Milstein | 1984 | Techniques of monoclonal antibody formation | Mouse, rat |
| Susumu Tonegawa | 1987 | Genetic principle of the generation of antibody diversity | Mouse |
| Jospeh E Murray, E Donnall Thomas | 1990 | Organ transplantation techniques | Dog, mouse, rabbit |
| Peter C Doherty, Rolf M Zinkernagel | 1996 | Immune system detection of virus-infected cells | Mouse, rat |
| Jules Hoffman, Bruce Beutler, Ralph Steinman | 2011 | Innate and adaptive immunity: Toll-like receptors and dendritic cells | Mouse |
| Tasuko Honjo, James P Allison | 2018 | Cancer therapy by checkpoint inhibition | Mouse |
| Katalina Kalikó, Drew Weissman | 2023 | mRNA vaccines (against COVID-19) | Mouse |

**) In total 115 Nobel prizes have been awarded between 1901 and 2024, whereby 101 prizes used animals in their research. Only examples in the field of Immunology are shown.*
*Source: https://www.animalresearch.info/en/medical-advances/nobel-prizes/*

Throughout the various phases of this initiative's development, additional input was provided by members of a sounding board group, consisting of immunologists from diverse disciplines and at different stages of their careers:

Joke den Haan
Rory de Vries
Jorge Dominguez Andres
Marije Koenders
Nienke Vrisekoop
Michiel van der Vlist
Febe van Maldegem
Ramon Arens
Peter Boross