SMA EUROPE

One Goal Series

Together We Discover

The SMA Europe Call for Research Proposals: from research investment to scientific progress

SMA
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YEARS

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Why long-term research investment still matters in SMA.

Reflections on twenty years of commitment and the road ahead.

Dr. Nicole Gusset Chief Executive Officer, SMA Europe
Dr. Yasemin Erbas President, SMA Europe

Over the past two decades, the spinal muscular atrophy (SMA) research landscape has undergone a profound transformation. Twenty years ago, no disease-modifying therapies were available and prospects were uncertain. Today, safe and effective treatments are part of clinical practice, genetic diagnosis is well established, newborn screening has been introduced and expanded across many countries, and multidisciplinary care has evolved significantly. At the same time, our understanding of the biology of SMA continues to advance rapidly, opening new possibilities for further progress. These achievements reflect the sustained efforts of researchers, clinicians, patient advocates, and families working together across borders and disciplines.

In 2026, SMA Europe marks its 20th anniversary. This milestone is both a moment of reflection and a call to responsibility. Progress in SMA research has been real and hard-won, but it has also brought new complexity. The existence of approved therapies is too often misinterpreted as the end of the research journey. For the SMA community, this assumption is both inaccurate and risky. Current treatments do not represent a cure, outcomes remain highly variable, and new and emerging challenges are increasingly reported across the lifespan. Continued research is therefore not optional: it remains essential.

Throughout its history, and particularly through its Calls for Research Proposals, SMA Europe has deliberately invested in research that is scientifically rigorous, patient-informed, and oriented towards long-term impact. This long-term commitment reflects the vision of the founders of SMA Europe, who recognised nearly two decades ago that sustained, patient-centred research investment would be essential to changing the trajectory of SMA. The Call is not designed to fund projects in isolation, but to strengthen a research ecosystem, one that links fundamental discovery, translational insight, and real-world relevance for people living with SMA.

Research supported by patient organisations, including SMA Europe and its members, has contributed to the scientific foundations that made today's therapies possible. By advancing understanding of disease mechanisms, identifying potential therapeutic targets, and supporting biomarker development and outcome measures, community-funded research has helped build the knowledge base upon which clinical advances depend. Such progress rarely follows a straight line. It unfolds step by step, study by study, often across different countries and laboratories, until a breakthrough becomes possible.

This is one of the reasons why coming together at European level matters. SMA is a rare disease, and expertise, ideas, and motivated researchers are distributed across borders. By pooling resources and aligning priorities, global collaboration enables support for excellent research wherever it takes place. Discoveries that benefit people living with SMA do not recognise national boundaries, and neither should our commitment to enabling them. The continued engagement of multiple member organisations and funders in the Call is therefore not only a question of financial scale, but of shared responsibility and collective vision.

This commitment to connection has also shaped recent awareness work of SMA Europe. Through the Connecting the Dots campaign, voices of people living with SMA were brought into dialogue with

researchers supported through the Call, highlighting how lived experience, scientific inquiry, and expectations continuously inform and challenge one another. These exchanges reinforce a core principle: meaningful research progress emerges when knowledge is connected across perspectives.

This report, "The SMA Europe Call for Research Proposals: from research investment to scientific progress" is published as part of the SMA Europe One Goal Series: Together We Discover. It represents a new step in how SMA Europe documents, connects, and communicates the outcomes of its research funding. Rather than presenting individual projects as stand-alone achievements, the report shows how knowledge accumulates over time, and how it creates a ripple effect. A funded project may generate new data, inspire follow-on studies, attract additional investment, inform clinical trial design, or contribute to improved care pathways. Impact extends beyond any single milestone, it grows through sustained effort and collaboration.

Importantly, this report does not claim to measure final impact. Research impact unfolds over years, often decades. Some of the work presented here has already influenced subsequent initiatives, while other contributions may only reveal their full significance in the future. Making this evolving trajectory visible, including progress made, challenges encountered, and questions that remain open, is part of SMA Europe's commitment to transparency, accountability, and learning.

As SMA Europe enters its third decade, sustained progress will depend on continuity: of funding, of expertise, and of collaboration. It will also depend on maintaining strong bridges between people living with SMA, researchers, clinicians, and decision-makers, ensuring that scientific advances remain aligned with community-defined needs and priorities. This report, and the broader One Goal Series, contributes to that shared endeavour.

The perspectives that follow, including reflections from the Chair of SMA Europe's Scientific Advisory Board, underline both how far the field has come and why continued, patient-centred research investment remains critical. Together, they reaffirm a shared goal: turning knowledge into lasting benefit for all people living with SMA.

Dr. Nicole Gusset, CEO

Dr. Yasemin Erbas, President

Anchoring Research Funding in Community Priorities

To ensure that its research funding addresses what matters most to people living with SMA, SMA Europe established a structured Priority Setting Partnership (PSP). Through a participatory process bringing together people living with SMA, caregivers, clinicians, and researchers, shared research priorities were identified, reflecting unmet needs across the SMA continuum and across the lifespan.

Learn more about the community-defined research priorities

These priorities provide a strategic reference point for Calls for Research Proposals of SMA Europe. They help guide funding decisions, support transparent prioritisation, and help ensure that limited resources are invested where they can generate the greatest relevance, legitimacy, and long-term value for the SMA community.

Scientific perspective. Interview with Prof. Tom Gillingwater, Chair of the Scientific Advisory Board of SMA Europe.

Tom Gillingwater graduated in Human Biology (Anatomy) from the University of Leeds and holds a PhD in Neuroscience from the University of Edinburgh. Since 2015, he has been Professor of Anatomy at the University of Edinburgh.

Tom is an elected Fellow of the Royal Society of Edinburgh (FRSE), Royal Society of Biology (FRSB), and Royal Microscopical Society (FRMS), an Honorary Fellow of the Anatomical Society (HonFAS), and a Member of the Scottish Medico-Legal Society.

To contextualise the impact of the Call for Research Proposals of SMA Europe within the rapidly evolving SMA research landscape, we spoke with Tom Gillingwater, Professor of Anatomy at the University of Edinburgh and Chair of the Scientific Advisory Board of SMA Europe since 2022. Drawing on more than two decades of experience in SMA research, he reflects on progress achieved, emerging risks, and the conditions required to translate discovery into lasting benefit for people living with SMA.

Could you please introduce yourself and describe your professional journey in SMA research?

My name is Tom Gillingwater. I am the Professor of Anatomy at the University of Edinburgh, where I am Head of the Department of Anatomy and also run a research group that explores the neuromuscular system in health and during disease. I first got interested in SMA when I was asked to use some of my anatomical skills to undertake an assessment of a newly-created mouse model of SMA, more than 20 years ago! What started as an initial "quick look" turned into a major aspect of my lab's research for nearly a quarter of a century. The SMA research field was very different back then (much more scientific and less clinical), so I have been privileged to witness (and perhaps contribute to, at least in a small way) the seismic shift that has occurred as we move into a world of effective therapies.

— What started as an initial "quick look" turned into a major aspect of my lab's research for nearly a quarter of a century —

From your perspective as a researcher, what have been the most significant achievements in the SMA field in recent years, and what do you see as the most pressing unanswered questions?

The obvious answer to the first part of your first question is the successful development and implementation of not just one, but three (!), effective therapies for SMA, with improvements every year in our understanding of how to best maximise their benefits to as many patients as possible. Newborn screening has contributed significantly to this effort, so I have watched on with envy as country after country roll out Newborn Screening for SMA, with the UK unfortunately being well behind the pack. The perhaps less obvious answer concerns the breakthroughs we've had in understanding the biology underlying SMA. There have been some incredible new studies published over recent years demonstrating how the SMN protein works, and why it is so important for the cells and tissues of the body. We know so much more than we did when I entered the field. With regards to unanswered questions, I feel that the 10 research priorities recently unveiled by SMA Europe are an excellent guide to many of the areas were research is critical. Amongst them, reflecting my own scientific interests, I would highlight a need for a better understanding of the requirements for SMN protein in a range of different tissues and organs over the lifespan, with a particular focus on what SMN does before birth. This will be really important for us to understand, and offer interventions designed to support, many of the new and emerging symptoms being reported in some SMA patients who have received SMN-restoring therapies.

Research is a core pillar of SMA Europe, which has supported numerous projects over the years through its Call for Research Proposals. Looking ahead, what do you see as the main challenges and expectations for SMA research? How can we best ensure that fundamental research discoveries are translated into meaningful clinical advances for people living with SMA?

I'm going to be brutally honest here: in my opinion the biggest risk is the severe drop in research funding that is available for SMA across the world (affecting both scientific and clinical research). Too many funding bodies now falsely believe that SMA is 'cured' and that their priorities should lie elsewhere. This is fundamentally wrong. The therapies we have are amazing, but we all know that they are a long way from representing a 'cure' for many people living with SMA. SMA Europe has been one of the few remaining institutions that continually supported SMA research, for which I (and many others) are incredibly grateful. However, if we are serious about addressing many of the issues confronting the SMA community, then increasing the funding available for SMA research is a must. Early career researchers are the lifeblood of any research field, and I worry greatly that the lack of funding in recent years has dramatically reduced the number of young people engaging with SMA research. No researchers: no research! On a brighter note, much of the SMA research that has managed to secure funding in recent years has significantly improved our understanding of the disease and the impact of disease-modifying therapies. As such, we are better placed than ever to deliver meaningful impacts for those living with SMA. There is considerable excitement around a range of second-generation therapeutic options that may become available alongside the current SMN-restoring therapies. We just need to provide the research infrastructure (people and funding) to ensure that these benefits are not delayed and can make it into the clinic as quickly as possible.

You have been first member and then, since 2022, Chair of the Scientific Advisory Board. What do you value most about your role?

SMA Europe is an incredibly important organisation that sits at the heart of European SMA advocacy, support and research activities. It brings together some wonderful people from all walks of life in order to do our best for people living with SMA and their families. It is genuinely an honour to be asked to be part of such an organisation, and I am very proud of what they/we have been able to achieve in recent years. I have been fortunate to be able to help select incredibly exciting research to fund through their grant calls (albeit with us always having to leave many excellent proposals unfunded) and to put together the programme for the international congress that is held every couple of years. It's at the congresses where you see the whole community coming together. That is a great feeling and something that I believe makes a real difference to the world of SMA and all those who are involved with it.

How do you think the role of patient advocacy organisations such as SMA Europe in collaborating with researchers has evolved in recent years? How can we encourage collaboration between patient advocates and researchers to ensure that the patient voice is meaningfully reflected in SMA research?

Open dialogue and mutual trust is key. SMA Europe has been at the forefront of driving patient-researcher relations for SMA and we are already seeing improved focus on key research areas as a result.

— Too many funding bodies now falsely believe that SMA is 'cured' and that their priorities should lie elsewhere. This is fundamentally wrong —

Projects funded through our **Call for Research Proposals**

2008
2024

6'091'034

€ total fundings

51 total projects

60 peer-reviewed publications

What is the Call for Research Proposals launched by SMA Europe?

The SMA Europe Call for Research Proposals is a recurring funding mechanism that supports high-quality scientific projects aimed at improving understanding of spinal muscular atrophy and advancing solutions that matter to people living with SMA. The Call primarily funds fundamental and translational research, including studies that explore disease mechanisms, therapeutic targets, biomarkers and biologically grounded aspects of care, with the objective of building knowledge that can inform future discoveries and benefit the community.

The Call exists to strengthen a collaborative research ecosystem that responds to community-defined priorities, accelerates scientific insight, and contributes to building the scientific foundations necessary for meaningful clinical progress.

+ info

Our next Call will be launched in 2026.

Call 12 2024

Principal Investigator	Institution	Title	Funding €
Gabriella VIERO	National Research Council, Trento, Italy	**Leveraging SMN role in translation to develop the next-gen of biomarkers for SMA**	121'500
Morgan GAZZOLA	I-Stem - Institute for Stem cell Therapy and Exploration of Monogenic diseases, Corbeil-Essonnes, France	**Deciphering the molecular landscape of neuromuscular development in spinal muscular atrophy**	150'000
Nathalie DIDIER	INSERM - Institut national de la santé et de la recherche médicale, Paris, France	**Skeletal muscle stem cells as untapped therapeutic targets for SMA long-term treatment (SATSMA)**	120'000
Sorana CIURA	Institut Imagine, Paris, France	**Investigating calcium-induced mitochondrial dysfunction in zebrafish and iPSC models of SMA**	90'000
Simon PARSON	University of Aberdeen, UK	**Are microvascular defects relevant in spinal muscular atrophy? Characterisation of the mouse model.**	98'110
Total			**579'610**

Dr. Morgan GAZZOLA

Deciphering the molecular landscape of neuromuscular development in spinal muscular atrophy

To improve care for people living with SMA, we need to better understand how the disease affects the body and to identify new biological mechanisms involved in its development.

Our ongoing project focuses on understanding how the loss of the SMN protein affects the development of the neuromuscular system, in particular at the neuromuscular junctions and which are the connections between nerves and muscles and are essential for movement.

To study this, we guide stem cells to develop into small three-dimensional structures called neuromuscular organoids. These models allow us to closely examine how SMA affects nerve–muscle communication during early development. Using this approach, we have observed that neuronal cells in SMA do not mature properly, suggesting that defects in early neuromuscular development may play an important role in the disease. By identifying new biological mechanisms and genes involved in SMA, our research aims to uncover new therapeutic targets. These could be used in combination with existing treatments to enhance their effectiveness.

— By identifying new biological mechanisms and genes involved in SMA, our research aims to uncover new therapeutic targets —

Dr. Nathalie DIDIER

Skeletal muscle stem cells as untapped therapeutic targets for SMA long-term treatment (SATSMA)

Skeletal muscle, the most abundant tissue in the body, is innervated by motor neurons to ensure essential functions such as breathing and walking. This tissue contains Muscle Stem Cells (MuSC) or satellite cells, which are necessary to maintain its integrity and repair it in case of injury. MuSC are also important to maintain the contact points between the motor neurons and the muscle (the neuromuscular junctions).

Since both muscle tissue and MuSC are affected in SMA, this project aims to better understand the interaction between MuSCs and motor neurons, and to investigate whether current therapies, in particular risdiplam, are able to reach MuSC and preserve their function. Our team discovered that MuSC need high levels of SMN to survive, and insufficient level of SMN in these cells can induce motor neuron death (Mecca et al., 2026).. Dr. Smeriglio's team, who's collaborating in this project, has shown that although risdiplam and nusinersen have a beneficial effect on muscle, they do not restore all the altered mechanisms. By deciphering how MuSC and motor neurons communicate, we aim to identify new therapeutic targets, to develop combined therapies that will improve and maintain muscle and the motor neuron function throughout patients' lives. By assessing the impact of current treatments on MuSC, we will provide crucial information for predicting the long-term impact of these treatments on the neuromuscular system.

— Since muscle stem cells are affected in SMA, this project aims to better understand their interaction with motor neurons, to identify new therapeutic targets —

Call 11 2022

Principal Investigator	Institution	Title	Funding €
Marina BOIDO	Neuroscience Institute Cavalieri Ottolenghi (NICO), Turin, Italy	**Uncovering the mechanism of action and synergistic potential of a SMA repositioned therapy**	150'000
Haiyan ZHOU	University College London (UCL), UK	**Investigating microvasculopathy in SMA patients and their response to nusinersen, onasemnogene abeparvovec and risdiplam**	149'639
Oliver GRUSS	Rheinische Friedrich-Wilhelms-Universität Bonn, Germany	**Nuclear and cytoplasmic phase separation enable novel functions of the SMN complex in RNP homeostasis.**	150'000
Simon PARSON	University of Aberdeen, UK	**Are vascular defects important in SMA?**	64'566
Peter CLAUS	SMATHERIA gGmbH, Germany	**Dysfunction of macrophages in spinal muscular atrophy (SMA)**	46'135
Total			**560'340**

Prof. Simon PARSON

Are vascular defects important in SMA?

I have been very interested in understanding if SMA affects more than only motor neurons. In this project, we have shown that blood vessels, which are present in every organ of the body, are damaged in SMA. Working with colleagues at Great Ormond St Hospital in London, we have investigated the effectiveness of current therapies on pathology in blood vessels.

We also hope to learn if additional combination therapies could be important for patients. Our findings could improve future therapies for SMA.

I am extremely grateful to SMA Europe for their funding and support. I have been able to interact with colleagues, people living by SMA and the public. This has improved and enhanced my appreciation of SMA and the need to keep researching.

— We have shown that blood vessels are damaged in SMA and investigated the effectiveness of current therapies on their pathology —

Prof. Haiyan ZHOU

Investigating microvasculopathy in SMA patients and their response to nusinersen, onasemnogene abeparvovec and risdiplam

Vascular health plays an important role in keeping the normal function of all organs in our body. In children living with SMA, Prof. Zhou and colleagues have discovered circulating biomarkers of endothelial injury and observed that the densities of capillaries are dramatically reduced in some organs examined, such as the retina (eye), skeletal muscle and spinal cord (Zhou et al., 2022). In this project, we seek to understand if the approved SMA therapies also improve vascular health. Our findings confirm the presence of neuroinflammatory cytokines in SMA and show that these are modulated in response to nusinersen (Zhang et al., 2024). We also identified promising vascular biomarkers and highlighted neuroinflammation as a potential contributor to disease pathology.

In parallel, we demonstrated that systemic SMN restoration with risdiplam fully rescues microvascular abnormalities in SMA mouse models, normalises endothelial biomarkers, and reverses molecular signatures linked to the inflammatory AGE–RAGE signalling and cytokine-driven inflammation. These findings establish microvasculopathy as a systemic and reversible hallmark of SMA and show that postnatal SMN restoration can effectively restore vascular health. This work supports the inclusion of peripheral vascular endpoints in future SMA clinical studies to better capture the multi-organ benefits of SMN-enhancing therapies. Together, these insights deepen our understanding of SMA's complex pathophysiology and may inform the development of more targeted therapeutic strategies.

— Our findings establish microvasculopathy as a systemic and reversible hallmark of SMA —

Prof. Marina BOIDO

Uncovering the mechanism of action and synergistic potential of a SMA repositioned therapy

This project, in collaboration with Prof. Artero (University of Valencia, Spain) and Dr Martinat (Inserm, I-Stem, France), aimed to identify a new treatment option for SMA by repurposing haloperidol, a drug already approved for other indications. Drug repurposing offers major advantages, as it relies on compounds with well-established safety profiles, known pharmacokinetics, and existing clinical use, thereby substantially reducing development time and costs compared to de novo drug discovery. Our study demonstrated that haloperidol improves survival and motor function in SMA, protects motor neurons from degeneration, and reduces harmful inflammation in the spinal cord. Treatment also improved muscle health and strengthened neuromuscular junctions, the connections between nerves and muscles that are severely affected in SMA. Importantly, haloperidol was shown to increase SMN protein levels and correct multiple downstream defects associated with SMA, acting through broader neuroprotective and anti-inflammatory mechanisms rather than solely through classical SMN splicing correction.

Because haloperidol is already clinically approved, these findings may help accelerate the path toward clinical testing, with the long-term goal of improving quality of life for people living with SMA across different disease stages. This work highlights the importance of continuing to explore complementary therapeutic strategies alongside existing treatments to address unmet needs in SMA. Projects like this are made possible through the sustained support of the SMA community, which plays a critical role in advancing research and translating scientific discoveries into tangible benefits for patients.

— We aimed to identify a new treatment option for SMA by repurposing haloperidol —

Call 10 2019

Principal Investigator	Institution	Title	Funding €
Peter CLAUS	Hannover Medical School, Germany	**A network-biology based approach for the development of SMN-independent treatments**	145'900
Christian SIMON	University of Leipzig, Germany	**Molecular mechanisms of synaptic transmission of the sensory motor-circuit in spinal muscular atrophy**	150'000
Monica NIZZARDO	Fondazione IRCCS Ca' Granda – Ospedale Maggiore Policlinico, Milan, Italy	**Unravelling the role of stathmin-2 in SMA as a key a key cause of motor neuron vulnerability and as a therapeutic target**	150'000
Lucia TABARES	University of Seville, Spain	**SMA: Mechanisms implicated in the perturbation of the calcium homeostasis and essay of a new therapeutic molecular target**	99'000
Total			**544'900**

Dr. Christian SIMON

Molecular mechanisms of synaptic transmission of the sensory motor-circuit in spinal muscular atrophy

Muscle weakness and paralysis are the most visible symptoms of SMA and for many years research focused mainly on the loss of motor neurons that control muscle movement. However, our work showed that another group of nerve cells, called proprioceptive neurons, which provide muscles with information about body position and movement, also contributed to movement problems in SMA. This project investigated whether changes in these sensory neurons could be used as a simple, non-invasive indicator of disease progression before and during treatment. We also examined how the connections between these neurons and motor neurons were affected by the disease. The results show that proprioceptive connections are affected in people with SMA, and treatments increasing SMN protein levels improve both movement and communication between sensory nerves and motor neurons, as detected by the Hoffmann reflex, a non-invasive clinical nerve test (Buettner et al., 2021; Simon et al., 2025). These findings open the possibility of using the Hoffmann reflex to monitor disease progression and treatment response in SMA. They also suggest that therapies aimed at improving proprioceptive function may help improve movement in SMA, even if they do not directly target the underlying genetic cause of the disease.

— We showed that proprioceptive connections are affected in people with SMA —

Prof. Lucia TABARES

SMA: Mechanisms implicated in the perturbation of the calcium homeostasis and essay of a new therapeutic molecular target

Our project aimed to understand how calcium signalling is altered in SMA and how these alterations contribute to motor neuron dysfunction. Calcium ions act as essential messengers inside nerve cells, controlling electrical activity, energy production, and communication between nerves and muscles.

We focused on motor nerve terminals, the specialised endings of motor neurons that activate muscles, which must carefully regulate calcium levels across different cellular compartments, including the cell membrane, cytosol, and mitochondria. We investigated how this delicate balance is disturbed in SMA and how this might weaken neuromuscular communication. We found that mitochondria in SMA motor nerve terminals uptake less calcium during nerve activity, implying a limitation in energy production, and so suggesting that energy failure and synaptic dysfunction are interconnected early events in the disease. We also showed that ribosomes and SMN proteins are present at motor nerve terminals and dynamically regulated during development, supporting a role for SMN in synaptic maturation and local protein synthesis. Together, these findings indicate that calcium dysregulation and mitochondrial stress are major contributors to early synaptic dysfunction in SMA, helping explain why neuromuscular junctions fail early in SMA, even before motor neurons are lost (Franco-Espin et al., 2022; Lopez-Manzaneda et al., 2021). This research opens new possibilities to: 1. protect neuromuscular communication, preserving muscle function for longer; 2. complement SMN-restoring therapies with treatments that stabilise nerve terminal physiology; 3. repurpose or inspire drugs that regulate electrical activity and calcium entry, an approach already used successfully in other motor neuron diseases. Altogether, this research supports the idea that maintaining synaptic health is a key therapeutic goal, for people with SMA.

This project highlights the importance of fundamental research in understanding disease mechanisms at the cellular level. Even as transformative therapies become available, basic science remains essential to explain why some neurons are more vulnerable than others and how long-term function can be preserved. Support from SMA Europe made it possible to explore innovative questions and technologies that continue to shape our understanding of SMA today.

— Our findings indicate that calcium dysregulation and mitochondrial stress are major contributors to early synaptic dysfunction in SMA —

Prof. Peter CLAUS

A network-biology based approach for the development of SMN-independent treatments

While approved treatments restore SMN levels, whose deficiency due to defects in a single gene causes SMA, not all patients benefit fully from these therapies, highlighting the need for additional treatment strategies. Our project aimed to identify novel mechanisms that contribute to motor neuron degeneration. In collaboration with Dr. Elia Di Schiavi (CNR, Naples, Italy), Prof. Dr. Niko Hensel (University of Halle, Germany), as well as several other research groups (e.g. Prof. Corti´s lab in Milan, Italy), we characterised proteins that become dysregulated even before motor symptoms appear. Network analyses revealed that these factors do not act independently but showed functional interactions. This led to the identification of suppressors and enhancers of the SMA phenotype. One key molecule identified was a protein which mediates signalling activity of many others, like a communication centre or hub. Modulation of this factor leads to beneficial effects in the SMA model (Hensel et al., 2021). Together, these findings highlight the importance of elucidating the molecular mechanisms underlying motor neuron degeneration in SMA. We are extremely grateful that SMA Europe has funded this project. There are still challenges in SMA field that need to be answered by research.

— Our project aimed to identify novel mechanisms that contribute to motor neuron degeneration —

Call 9 2016

Principal Investigator	Institution	Title	Funding €
Tom GILLINGWATER	University of Edinburgh, UK	**Defining the role of the motor axon translatome in SMA pathogenesis**	147'800
Min Jeong KYE	University of Cologne, Germany	**Restoring disturbed energy homeostasis in SMA motor neurons**	150'000
Laura TORRES-BENITO	University of Cologne, Germany	**Combinatorial ASO therapy using SMN-dependent and SMN-independent protection against SMA**	60'000
Total			**357'800**

Call 8 2015

Principal Investigator	Institution	Title	Funding €
Simon PARSON	University of Aberdeen, UK	**Determining the temporal, spatial and molecular signature of hypoxia in spinal muscular atrophy**	109'293
Suzie LEFEBVRE	INSERM Paris Decartes, France	**Role of a redox sensor in nuclear organisation and its implication in spinal muscular atrophy**	73'000
Frederic ALLAIN	ETZ, Zurich, Switzerland	**Seeking small molecules that stabilise protein RNA interactions to cure spinal muscular atrophy**	150'000
Olga TAPIA	Cantabria University, Santander, Spain	**Regulation of the Survival Motor Neuron (SMN) protein by acetylation and its importance in snRNP biogenesis and molecular assembly of cajal bodies**	40'000
Niko HENSEL	Hannover Medical School, Germany	**The ROCK-ERK signalling network in SMA - mediator of neurodegeneration and SMN independent treatment target**	100'000
Total			**472'293**

Prof. Olga TAPIA

Regulation of the Survival Motor Neuron (SMN) protein by acetylation and its importance in snRNP biogenesis and molecular assembly of cajal bodies

This project focused on understanding how histone deacetylase inhibitors (HDAC inhibitors) affect motor neurons in SMA at the cellular level. At the time, HDAC inhibitors were being explored as potential therapeutic agents because of their ability to increase SMN expression; however, their direct impact on motor neuron biology and nuclear organization was poorly understood.

This project demonstrated that the SMN protein is directly regulated by post-translational modifications that critically determine its function inside the cell (Lafarga et al., 2018; Tapia et al., 2017). We identified the acetyltransferase CBP as a specific enzyme that acetylates SMN at a residue within a domain essential for its interactions. This acetylation altered RNA splicing. In contrast, an acetylation-defective SMN mutant promotes the formation of abnormal nuclear microbodies, identifying SMN acetylation as a molecular switch that controls its nuclear compartmentalisation.

These findings provided a mechanistic explanation for why histone deacetylase inhibitors, despite increasing SMN levels, show limited therapeutic efficacy in SMA: SMN quantity alone is not sufficient, and preservation of its correct nuclear regulation and function is essential for motor neuron integrity.

This project laid the foundation for my independent research line in SMA, illustrating how funding at an early stage can consolidate a long-term research programme, generating sustained impact beyond a single study and continuing to contribute to the understanding of SMA mechanisms and therapeutic responses.

— This project demonstrated that the SMN protein is directly regulated by post-translational modifications that critically determine its function —

Dr. Niko HENSEL

The ROCK-ERK signalling network in SMA - mediator of neurodegeneration and SMN independent treatment target

I received two grants by SMA Europe: a postdoctoral fellowship in 2016, during which we evaluated the impact of two repurposed drugs in SMA, and a research grant in 2020 awarded in collaboration with Peter Claus (Hannover, Germany) and Elia Di Schiavi (Naples, Italy) where we tried to identify new ways to ameliorate SMA symptoms. Both grants had the long-term goal to identify treatment options that go beyond increasing SMN levels.

Through this work, we showed that motor neurons and other cell types process information differently in SMA, revealing a whole network of altered information flow. This helped us identify central network nodes that we believe are important switches influencing disease phenotypes, potentially in ways independent of SMN (Hensel et al., 2017; Hensel et al., 2021; Tapken et al., 2025).

Despite the current availability of disease-modifying therapies, significant unmet needs remain for people living with SMA. Future generations of therapies will be required that do not rely solely on increasing SMN levels and that can be used in combination with SMN-enhancing drugs. We hope that our holistic approach to mapping large regulatory networks will contribute to the identification of such novel treatment strategies.

SMA Europe funded my work and my positions at critical times of my scientific career. This allowed me to remain in SMA research and ultimately establish my own research group. Today, we are a small but growing team of dedicated researchers based in Halle (Germany), working to better understand SMA and, ultimately, to improve outcomes for patients.

— We showed that motor neurons and other cell types process information differently in SMA —

Call 7 2014

Principal Investigator	Institution	Title	Funding €
Ruben ARTERO	Universitat de València, Spain	**A spinal muscular atrophy drosophila model for in vivo drug discovery**	121'500
Martine BARKATS	INSERM-UPMC-Institut de Myologie, Paris, France	**Study of the role of SMN in the regulation of muscle-resident progenitors for the identification of novel therapeutic targets for SMA**	124'000
Francesco MUNTONI	University College London, UK	**Identification of microRNAs as biomarkers and potential therapeutic targets in spinal muscular atrophy**	108'000
Total			**353'500**

Call 6 2013

Principal Investigator	Institution	Title	Funding €
George MENTIS	Columbia University, NY, USA	**Cellular basis of motor circuit dysfunction induced by SMN deficiency**	150'000
Eduardo TIZZANO	Hospital de la Santa Creu i Santa Pau, Barcelona, Spain	**Modulating SMN2 splicing with dual inhibitors of Sam68 ans hnRNP A1: A novel therapeutic approach for spinal muscular atrophy**	117'500
Amparo GARCIA-LOPEZ	University of Geneva, Switzerland	**Using RNA secondary structure as a therapeutic target for spinal muscular atrophy**	122'500
Total			**390'000**

Prof. George MENTIS

Cellular basis of motor circuit dysfunction induced by SMN deficiency

The project (funded for the period 2013-2015) studied how interneurons interact with spinal motor neurons under SMA conditions. One of the fundamental questions that was addressed was whether death and dysfunction of motor neurons – both events are hallmarks of SMA – are closely associated or occur via different mechanisms. This was a critical question to be addressed and would have important implications for therapies, since in a mouse model of SMA, dysfunction in motor circuits as a whole was reported to be one of the earliest manifestations of the disease, preceding motor neuronal death.

At the period when the project was proposed, death and dysfunction of motor neurons in SMA were long considered to be solely as a cell-autonomous problem. However, in collaboration with Livio Pellizzoni, we found that these two major pathological events in SMA – dysfunction and death of motor neurons – are uncoupled!

The project demonstrated that SMN deficiency induces selective motor neuron death through cell-autonomous mechanisms, while hyperexcitability (a form of dysfunction) is a non-cell-autonomous response of motor neurons to defects in pre-motor interneurons, leading to loss of glutamatergic synapses and reduced excitation (Simon et al., 2016). Results suggested that dysfunction and death of motor neurons are the outcomes from differential effects of SMN deficiency in distinct neurons of the motor circuit and that dysfunction does not trigger motor neuron death.

Subsequent work from the Mentis laboratory and collaborators further demonstrated that proprioceptive sensory neurons are key players in mediating motor neuron dysfunction in SMA (Fletcher et al., 2017; Simon et al., 2025). Dr Mentis also joined the efforts of Dr Marco Capogrosso (University of Pittsburgh), who used epidural stimulation in three SMA Type 3 patients and reported remarkable benefits by increasing muscle strength, reducing fatigue and improving gait as some of the behavioural benefits (Prat-Ortega et al., 2025). Current efforts are focused in determining the long-term benefits of epidural stimulation as a combined therapy to the currently approved SMA therapies.

— We found that dysfunction and death of motor neurons are uncoupled events —

Call 5 2012

Principal Investigator	Institution	Title	Funding €
Martine BARKATS	Institut de Myologie, INSERM, Paris, France	**Optimisation of AAV9-SMN gene therapy for SMA**	192'764
Frederic ALLAIN	ETH Zürich, Switzerland	**In search of small molecules targeting protein-RNA complex: a novel approach against spinal muscular atrophy**	80'000
Shingo KARIYA	Columbia University, NY, USA	**Elucidate the molecular mechanism underlying maturation and remodelling defects of the neuromuscular system in SMA**	124'314
Total			**397'078**

Call 4 2011

Principal Investigator	Institution	Title	Funding €
Tilman ACHSEL	Center for the Biology of Disease, KU Leuven, Belgium	**mRNA transport in SMA pathogenesis**	142'100
Mathew WOOD	Oxford University, UK	**Delivery of splice switching oligonucleotides using exosomes for the treatment of spinal muscular atrophy**	149'905
Umrao MONANI	Columbia University, NY, USA	**Investigating novel genetic determinants of the SMA phenotype**	141'455
Markus RIESSLAND	University of Cologne, Germany	**Spinal muscular atrophy: molecular and functional analysis of a new modifier of SMA**	124'000
Yannick TANGUY	INSERM, Paris, France	**AAV9- medaited gene therapy in murine models of SMA**	97'068
Total			**654'528**

Prof. Umrao MONANI

Investigating novel genetic determinants of the SMA phenotype

This project sought to reveal novel genetic modifiers of SMA, to better understanding the biology underlying the disease and to identify potential therapeutic targets to treat SMA.

The project led to the identification of a novel genetic suppressor of SMA, a synaptic chaperone. Proof-of-concept work also demonstrates the feasibility of exploiting the modifier or related molecules as therapeutic agents for the treatment of SMA (Kim et al., 2023).

I was fortunate that SMA-Europe funded an idea worth exploring at a relatively early stage. The final outcomes of the project are of considerable significance. This is an example of an investment in a risky project that paid off handsomely.

— We identified a novel genetic suppressor of SMA, a synaptic chaperone —

Call 3 2010

Principal Investigator	Institution	Title	Funding €
Martine BARKATS	INSERM, Paris, France	**AAV9-mediated gene therapy in murine and feline models of SMA**	164'725
David SATTELLE	University of Manchester, UK	**New drugs and new drug targets for spinal muscular atrophy using chemical and functional genomics**	74'575
Kathleen MAHIAS	INSERM, Lille, France	**Evalation of the contribution of *SMN1* and *SMN2* sequence variants to the clinical severity of SMA**	82'750
Sandra DUQUE	The Ohio State University, Columbus, USA	**Delivery and correction of SMA using AAV vectors**	51'000
Total			**373'050**

Call 2 2009

Principal Investigator	Institution	Title	Funding €
Umrao MONANI	Columbia University, NY, USA	**Investigating the temporal requirements of the SMN protein in spinal muscular atrophy**	122'513
Mimoun AZZOUZ	University of Sheffield, UK	**PTEN modulation effects on motor neuron axonal growth and neuromuscular junction size in spinal muscular atrophy**	61'060
Steve WILTON	University of Western Australia	**Antisense oligomer induced restoration of SMN expression as a therapy for spinal muscular atrophy**	146'150
Remy BORDONNÉ	IGMM-Molecular Genetics Institute of Montpellier, France	**The *S. pombe* model organism: a tool to find suppressors of snRNP-mediated splicing defects**	110'000
Béatrice JOUSSEMET	Université de Nantes, France	**Evaluation of new AAV-mediated gene therapy strategies in a feline model of spinal muscular atrophy**	65'000
Rachel NLEND NLEND	Universität Bern, Switzerland	**Gene therapy for spinal muscular atrophy by a correction of *SMN2* MRNA splicing**	65'000
Claudia FALLINI	Emory University, USA	**Analysis of mRNA transport and local protein syntheses in axons of SMA motor neurons**	65'000
Total			**634'723**

Dr. Remy BORDONNÉ

The S. pombe model organism: a tool to find suppressors of snRNP-mediated splicing defects

Our team used the *Schizosaccharomyces pombe* model organism to analyse the in vivo role of SMN in snRNP biogenesis and splicing. Fission yeast is of particular interest to study these processes because it contains a splicing machinery close to mammals in both similarity and content. We showed that SMN is directly required for the in vivo stability of the spliceosomal snRNAs associated with the Sm core complex. We also found that some introns are more sensitive to low snRNP levels than others and that splicing of approximately 10% of introns is preferentially inhibited in SMN-depleted cells. Similar defects have also been identified in fission yeast cells carrying a deletion in a component of the methylosome, a protein complex essential for ssplicing (Barbarossa et al., 2014). Our data are consistent with the notion that splice site selection and spliceosome kinetics are highly dependent on the concentration of core spliceosomal components. Our studies should provide important results in exploring new pathways able to supress or compensate defects induced by mutations in the SMN gene.

— SMN is directly required for the in vivo stability of the spliceosomal snRNAs associated with the Sm core complex —

Prof. Umrao MONANI

Investigating the temporal requirements of the SMN protein in spinal muscular atrophy

This project sought to determine when, during life, the SMN protein is most critically required to ensure the health of the neuromuscular system and prevent symptoms of SMA. The rationale was that outcomes would inform the timing of SMA treatments that were being developed at the time. The project determined that the SMN is most critically required during early postnatal life when the neuromuscular system is maturing and being refined. From this it was inferred that future treatments for SMA would have to be administered at the very earliest time points possible. The project also determined that the requirements for the SMN protein were radically reduced during adulthood but injury to neuromuscular connections triggered a surge in requirement for the protein (Kariya et al., 2014; Lutz et al., 2011).

— SMN is most critically required during early postnatal life when the neuromuscular system is maturing and being refined —

Call 1 2008

Principal Investigator	Institution	Title	Funding €
Margarida GAMA CARVALHO	University of Lisbon, Portugal	**Characterisation of post-transcriptional control mechanisms regulating SMN2 gene expression**	85'760
Eugenio MERCURI	Università Cattolica, Rome, Italy	**Outcome measures in SMA types II and III**	276'000
Giacomo Pietro COMI	University of Milan, Italy	**Development of a stem cell approach for treating spinal muscular atrophy**	120'000
Martine BARKATS	Institut de Myologie, Paris, France	**Evaluation of AAV-mediated gene therapy in murine and feline SMA models**	211'452
Monir SHABABI	University of Missouri, USA	**A two-pronged approach to develop a treatment for spinal muscular atrophy**	80'000
Total			**773'212**

Publications and emerging impact

Research impact unfolds gradually and often in unexpected ways. Studies funded through the SMA Europe Call for Research Proposals contribute to an evolving body of knowledge that may inform follow-up projects, attract additional funding, strengthen collaborations across institutions, refine methodologies, support biomarker development, or shape future therapeutic strategies and clinical trial design. Particularly in fundamental and translational research, progress is rarely immediate or linear but its influence can extend well beyond the original project scope and become visible only over time.

Among the more tangible outcomes of this process are peer-reviewed scientific publications. These publications represent validated contributions to the scientific evidence base, ensuring that findings are critically assessed, openly shared, and integrated into ongoing research efforts worldwide. While publications capture only part of the impact, they provide a transparent and traceable record of knowledge generated through the Call.

The following bibliography lists peer-reviewed publications resulting from projects supported by SMA Europe. Together, they illustrate how sustained research investment contributes to scientific progress and lays foundations for future advances in SMA.

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