The first predictive in vitro assay for the identification of respiratory sensitizers.

Informe

Información del proyecto

GARDair

Identificador del acuerdo de subvención: 756014

Sitio web del proyecto

DOI
10.3030/756014

Proyecto cerrado

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SOCIETAL CHALLENGES - Health, demographic change and well-being

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Aportación de la UE
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Coordinado por
SENZAGEN AB
Sweden

Periodic Reporting for period 2 - GARDair (The first predictive in vitro assay for the identification of respiratory sensitizers.)

Período documentado: 2018-03-01 hasta 2019-08-31

Resumen del contexto y de los objetivos generales del proyecto

Chemical sensitization, also referred to as chemical allergy, is a disease state induced by the human immune system in response to chemical sensitizers. Sensitized individuals that are subsequently exposed to such chemicals will suffer from disease-associated symptoms, such as itching, blistering and tissue damage in case of skin contact, and coughing, wheezing and asthma-like symptoms in case of inhalation.

It is well recognized that the route of exposure may have an impact on the observed symptoms. However, it is also becoming increasingly clear that chemical compounds may have intrinsic properties that preferentially lead to sensitization of the skin or the respiratory tract, also referred to as allergic contact dermatitis (ACD) and occupational asthma (OA), respectively. This understanding has an impact on how chemicals are safety tested and labeled for potentially hazardous effects.

In both cases, these kinds of safety assessments have historically been carried out using animal experiments. However, public opinion, concern for human environmental health and economic interests have lead to legislations within the EU that prohibits the use of animal experiments to perform safety assessments on cosmetics and any ingredients thereof, a trend that is currently spreading both globally and across market and industry segments. Thus, there is an urgent need to develop animal-free methods for assessment of chemical sensitizers. While several animal-free, so called in vitro assays for assessment of skin sensitizers have been proposed, the demand for an assay that accurately and specifically predicts and classifies chemical respiratory sensitizers remains unfulfilled.

SenzaGen AB, the beneficiary of this Horizon 2020 grant, specializes in the development of in vitro methods for assessment of immunotoxicological endpoints. Specifically, in order to meet the demand of specific and accurate assessment of chemical respiratory sensitizers, the novel assay GARDair was developed, designed as an independent application of the GARD – Genomic Allergen Rapid Detection – technology platform. Industrial implementation of the proposed methodology required substantial resources, which were granted to the beneficiary by Horizon 2020. Within the context of the herein reported project, substantial progress towards the specific objectives have been made.

As of this reporting, the project has been successfully completed. The project has generated scientific evidence of the validity and functionality of the proposed methodology, as well as novel hypotheses potentially able to fill current knowledge gaps in the field of chemical respiratory sensitization. A finalized assay has been established with standardized operating procedures, based on a technological format suitable for industrial implementation. The assay has been successfully transferred to naïve laboratories participating in an inter-laboratory ring trial, demonstrating that the method is reproducible and predictive, as compared to existing counterparts available for skin sensitization. Lastly, technical achievements have been appropriately exploited in order to maximize gain both for the beneficiary and for society.

In summary, the successful completion of this project has led to the finalization of GARDair, a novel

method for assessment of chemical respiratory sensitizers. GARDair is currently offered as part of the SenzaGen product portfolio, and is readily available on the market.

Trabajo realizado desde el comienzo del proyecto hasta el final del período abarcado por el informe y los principales resultados hasta la fecha

The first period of the project focused on R&D activities. The overall goal has been to identify and confirm the validity of genomic biomarkers for respiratory sensitization and irritation, and the application of such genomic biomarkers in the design of predictive assays for the respective biological endpoints. Whole genome analysis was utilized in order to identify predictive gene signatures, which in turn were implemented in predictive models based on machine-learning techniques.

The second period of the project focused on technical applications of these findings in a technical format suitable for industrial application. Prediction models were finalized, software for data analysis was constructed and standard operating procedures of the finalized methodology were established. Furthermore, the finalized assay was transferred to naïve laboratories in order to conduct an inter-laboratory ring trial, generating data sufficient for eventual regulatory acceptance, as well as providing early estimates of assay performance.

Throughout the project, continuous efforts have been made to enhance the SenzaGen commercial organization in order to appropriately exploit generated results. Analyses of markets, private and regulatory stakeholders and project impact have been continuously monitored and implemented within the organization. Project results were continuously reported to the scientific community, clients, partners and investors through written reports, presence at conferences and social media activities. Marketing material has been created, aimed for various target groups and key opinion leaders. All relevant findings from the project have been adequately protected in terms of intellectual property and potential leads for future licensing of the technology to partner laboratories have been secured.

Avances que van más allá del estado de la técnica e impacto potencial esperado (incluida la repercusión socioeconómica y las implicaciones sociales más amplias del proyecto hasta la fecha)

According to current legislations within the EU, testing of a chemical's ability to induce respiratory sensitization is to be performed if relevant and possible, with methods approved for the specific purpose. However, no such methods exist. Still, while not approved for regulatory use and registration, various assays based on animal experimentation have been proposed. However, the usage of such methods conflicts with current recommendations to use primarily in vitro methods to assess sensitization. Thus, the current state of the art is considered to be at baseline level.

It is expected that the GARDair project will advance the current state of the art by I) demonstratating the functionality and applicability of a novel technology for assessment of respiratory sensitizers, thus

fulfilling European legislations and recommendations previously not achieved, and II) advancing said legislations to better reflect the current technological state of the art.

The proposed technology has the potential to not only save thousands of animal lives, but also to provide a broad spectrum of industries with an affordable and more accurate alternative to current animal-based methods. Ultimately, the GARD technology will contribute to technical and regulatory progress in this domain.

In conclusion, the project is expected to have a profound impact on various aspects of society. Examples include, but are not limited to, the technological advancement of the state of the art, allowing for safe and resource effective product development in chemical- and pharma-associated industries, animal welfare, increased environmental health and quality of life in sensitized individuals, which in turn contributes to the alleviation of economic burdens associated with disease.

SenzaGen Logo on backdrop

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