omvac otitis media vaccine	Project title Novel prevention and treatment possibilities for Otitis Media through comprehensive identification of antigenic proteins		
Instrument	Specific Targeted Project	Acronym	OMVac
Thematic priority	Integrating and strengthening the European Research Area	Project no.:	037653

Nonconfidential summary
OMVac 037653

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Project coordinator name		Martin B. Oleksiewicz	
Project coordinator organisation name		Intercell AG	

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Abbreviations:

Mcat: Moraxella catarrhalis
NTHi: Nontypeable Haemophilus influenzae
OM: Otitis media
ORF: Open reading frame

1 SUMMARY

The main goal of the OMVAc project was the identification of candidate *Moraxella catarrhalis* (Mcat) and non-typeable *Haemophilus influenzae* (NTHi) protein antigens suitable for the development of a prophylactic vaccine to prevent otitis media in children.

The OMVac project succeeded in identifying and filing patent applications for a large set of Mcat and NTHi protein antigens.

Based on serological, genetic, bioinformatic and patentability-based antigen validation, NTHi and Mcat proteins were generated in pure, recombinant form for efficacy testing

in preclinical animal models. The OMVac antigens were compared with previously published benchmark proteins in preclinical mouse models, and lead candidates were identified that performed better than the benchmark proteins or killed bacteria (the latter a strong positive control in mouse models). Thus, the NTHi and Mcat antigens identified under OMVac appear to compare favourable with state-of-the-art benchmark antigens.

In parallel activities, the NTHi and Mcat protein antigens were validated by molecular microbiology means (eg generation of gene deletion knockouts and functional protein studies), and the human immune responses directed against these antigens during otitis media were examined.

Thus, in short, OMVac reached the major objective: The project identified and filed patent applications for new NTHi and Mcat protein antigens.

OMVac was not intended to deliver a complete preclinical package for all identified NTHi and Mcat antigens. A substantial amount of work is still needed to generate the preclinical efficacy and safety data necessary for eg clinical entry of the NTHi and Mcat antigens identified under OMVac. This post-OMVac preclinical antigen development is currently ongoing, based on the solid knowledge and network foundation provided by the OMVac project.

2 PROJECT EXECUTION

2.1 OBJECTIVES, CONTRACTORS, LOGO AND WEB SITE

2.1.1 Project objectives

Otitis media (OM) is a prevalent disease of children, affecting most children by the age of 3. Due to the high prevalence and potentially serious consequences, OM thus constitutes a major burden to children, parents and public health systems. While otitis media is a multifactorial disease, with predisposing contributions from the environment, viral pathogens and genetic factors, three bacterial pathogens are recognized as main causes of the disease: *Streptococcus pneumoniae* (pneumococcus), non-typeable *Haemophilus influenzae* (NTHi) and *Moraxella catarrhalis* (Mcat).

Pneumococcus is considered the main OM pathogen, with NTHi and Mcat currently thought to be responsible for 35-50% and up to 20%, respectively, of acute otitis media cases. Solid evidence is lacking that antibiotics alter the course of OM disease in children. Also, development of antibiotic resistance in all three OM pathogens has been documented. For these reasons, and due to the high burden of disease, there is a medical need for improved OM prophylaxis, which could be afforded by OM vaccines. The literature supports that there is good reason to believe that development of a prophylactic OM vaccine is feasible and biologically plausible, provided the right antigens can be found. This formed the basis for the OMVac project.

Based on the medical situation outlined above, and current scientific knowledge about OM pathogenesis, the OMVac project objectives were defined thus in the technical annex: "The OMVac project addresses as main objectives the identification of vaccine candidates from *Moraxella catarrhalis* (Mcat) and non-typeable *Haemophilus influenzae* (NTHi) to develop a prophylactic vaccine against otitis media and the comprehensive characterisation of natural immune responses against proteinaceous antigens of the major three bacterial pathogens causing OM".

2.1.2 Contractors

The 7 OMVac contractors are listed below.

For detailed contractor information, including links to contractor's web sites, please see the OMVac web site.

- Participant 1: Intercell AG (IC)
  Dr. Martin B. Oleksiewicz, DVM, PhD

- Participant 2: Agowa (AW)
  Dr. Wolfgang Zimmermann and Dr. Steffen Krüger

- Participant 3: University of Graz, Institute of Pharmaceutical

Sciences, Department of Pharmaceutical Chemistry (UG)
Professor Dr. Andreas Kungl

- Participant 4: 2nd Department of Pedatrics, Semmelweis University (PS)
  Dr. Éva Ban

- Participant 5: Erasmus Medical Center, Department of Medical Microbiology & Infectious Disease (EMC)
  Dr. John P. Hays

- Participant 6: Radboud University Nijmegen Medical Centre (RUNMC)
  Professor Dr. Peter W. Hermans

- Participant 7: Karolinska Institutet (KI)
  Professor Dr. Birgitta Henriques-Normark

2.1.3 OMVac web site

During the second project period, an OMVac web site was opened.

The site is managed by partner 1 (Intercell AG), and is expected to run for approximately 2 years after completion of the OMVac project, to ensure dissemination of eg scientific publications completed by partners after the formal completion of the OMVac project.

The OMVac web site can be found at:

www.omvac.org

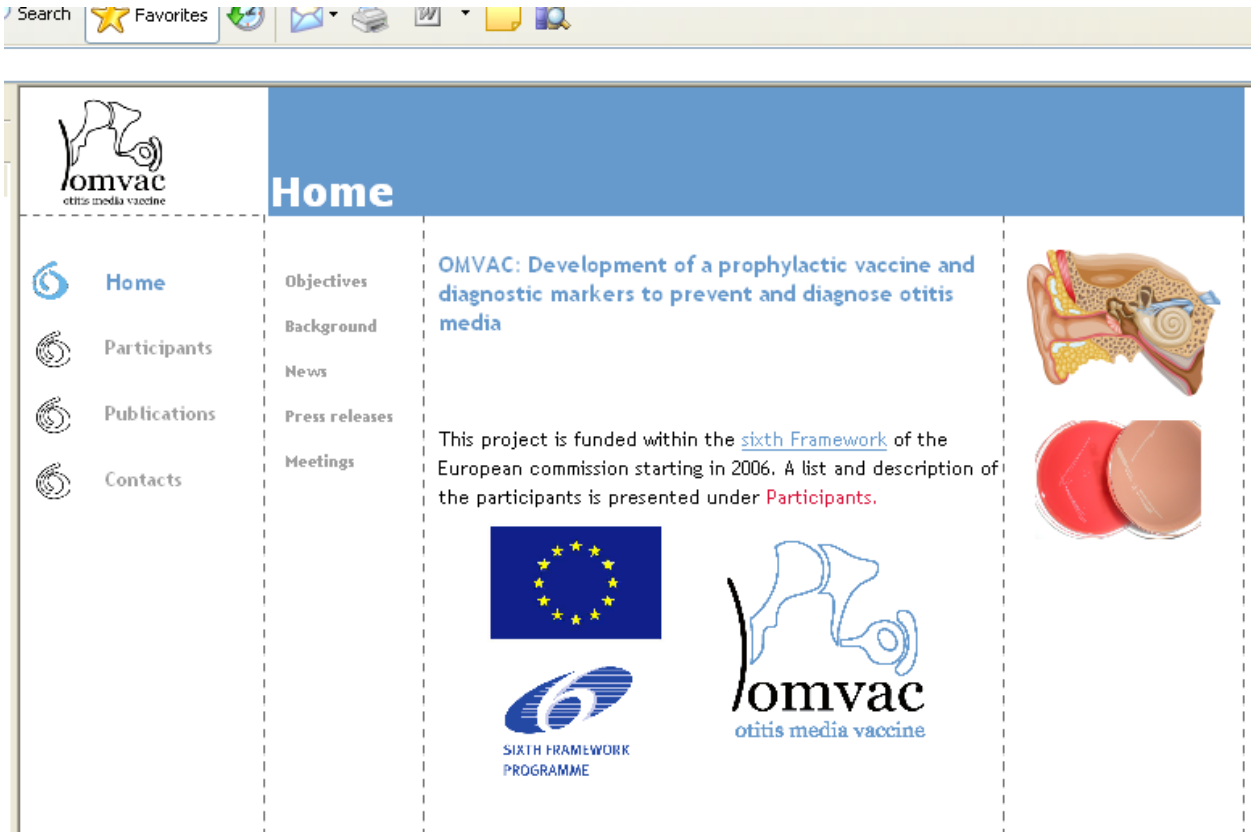

Figure 1. Screenshot of OMVac project web page (www.omvac.org)

2.1.4 Logo

An official OMVac logo was approved by the consortium meeting in Vienna 2-3 June 2009.

The official OMVac logo is shown in figure 2. It can be copied from the OMVac web site (www.omvac.org), and is available on request from the project coordinator (Intercell AG).

At the consortium meeting in Vienna on 2-3 June 2009, the logo's designers (partners 2 and 6, Agowa and RUNMC) approved the free use of the logo by all consortium members for all OMVac-related material.

Figure 2. Official OMVac logo

2.2 OMVAC ACHIEVEMENTS AND STATE-OF-THE-ART

A number of NTHi candidate vaccine antigens have been identified previously. However, as regards protein-based vaccine antigens, these candidate antigens comprise essentially the 10 most abundant NTHi surface proteins (Cripps AW, Otczyk DC, 2006. Expert Rev Vaccines 5: 517-34. Murphy, T.F., 2005. Expert Rev Vaccines 4: 843-53). Similarly, a number of candidate Mcat vaccine antigens have been identified, but these approximately 15 candidate antigens comprise essentially a sample of the most abundant Mcat surface proteins (Murphy, T.F., 2005. Expert Rev Vaccines 4: 843-53. Mawas F., et al., 2009. Expert Rev. Vaccines 8: 77-90).

Thus, it appears very likely that more and potentially better vaccine candidate antigens based on NTHi and Mcat proteins can be found, by new, systematic antigen discovery methods. This formed the basis for the OMVac project.

Under OMVac, a large panel of NTHi and Mcat proteins was in fact identified and patent applications filed.

Furthermore, the NTHi and Mcat antigens identified under OMVac have been compared with clinically evaluated or published benchmark proteins in preclinical mouse models, and for both NTHi and Mcat proteins identified under OMVac, lead candidates have been identified that performed better than those clinically evaluated or published benchmark NTHi and Mcat proteins. In fact, for NTHi proteins identified under OMVac, lead candidates have been selected that performed as well as or better than inactivated bacterial antigen (a strong positive control in mouse models).

Thus, the OMVac project achieved the main objective, the identification of vaccine candidates from *Moraxella catarrhalis* (Mcat) and non-typeable *Haemophilus influenzae* (NTHi) to develop a prophylactive vaccine against otitis media. As described above, the OMVac achievement is considered to compare favourable to and offer advantages above the current state-of-the-art as regards NTHi and Mcat antigens.

2.3 PUBLISHABLE RESULTS

It is to be expected that in a large project such as OMVac, final data analysis and finalization of scientific publications will not be completed by the formal project end date, and that these activities will go on beyond the formal project end date.

Therefore, at the final consortium meeting (Budapest 22-23 February 2010), focus was placed on agreeing on a strategy for post-OMVac publication plans of OMVac-related data. The consortium decided that it will try to combine data across workpackages to make maximum-impact publications (ie, fewer maximum-impact publications will be favoured over more lower-impact publications).

The results that will be published post-OMVac were derived from all workpackages, and several OMVac-related publications are expected in the future, comprising animal model development, NTHi and Moraxella antigen identification and validation, and description of eg immune responses in children with otitis media. Based on the quality of available data, the increased publication activity and track record in the second period (please see table 3), and the benefit of scientific peer-reviewed publications in the ongoing continued preclinical development of NTHi and Mcat antigens, it is thought that this projection of several OMVac-related publications in the future is very realistic.