

# The AsthmaMap: computational representation of disease mechanisms using domain expert knowledge

Alexander Mazein<sup>1,\*</sup>, Olga Ivanova<sup>1,2,3</sup>, Irina Balaur<sup>1</sup>, Valeriya Berzhitskaya<sup>4</sup>, Tatiana Serebriyskaya<sup>4</sup>, Bertrand De Meulder<sup>1</sup>, Richard G. Knowles<sup>5</sup>, Craig Wheelock<sup>6</sup>, Sven-Erik Dahlen<sup>6</sup>, Kian Fan Chung<sup>7</sup>, Ian Adcock<sup>7</sup>, Graham Roberts<sup>8,9</sup>, Anke-Hilse Maitland-van der Zee<sup>3</sup>, Josep Roca<sup>10</sup>, Johann Pellet<sup>1</sup>, Piotr Gawron<sup>10</sup>, Stephan Gebel<sup>11</sup>, Marek Ostaszewski<sup>11</sup>, Reinhard Schneider<sup>11</sup>, Rudi Balling<sup>11</sup>, Peter J. Sterk<sup>3</sup>, Charles Auffray<sup>1,\*</sup>; U-BIOPRED Study Group; eTRIKS Working Group

<sup>1</sup> European Institute for Systems Biology and Medicine, CIRI UMR5308, CNRS-ENS-UCBL-INSERM, Université de Lyon, 50 Avenue Tony Garnier, 69007 Lyon, France; <sup>2</sup> Vrije Universiteit Amsterdam, De Boelelaan 1105, 1081 HV Amsterdam, The Netherlands; <sup>3</sup> Respiratory Medicine, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands; <sup>4</sup> Moscow Institute of Physics and Technology, 9 Institutskiy Pereulok, Dolgoprudny, Moscow Region, 141700, Russia; <sup>5</sup> Knowles Consulting, Stevenage Bioscience Catalyst, Gunnels Wood Road, Stevenage SG1 2FX, UK; <sup>6</sup> Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden; <sup>7</sup> National Heart & Lung Institute, Imperial College London, London SW3 6LY, UK; <sup>8</sup> University of Southampton, Southampton, UK; <sup>9</sup> NIHR Southampton Biomedical Research Centre, Southampton, UK; <sup>10</sup> Hospital Clinic of Barcelona, Carrer de Villarroel, 170, 08036 Barcelona, Spain; <sup>11</sup> Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg, Campus Belval, 7 Avenue des Hauts-Fourneaux, L-4362 Esch-sur-Alzette, Luxembourg; \* Corresponding authors

**BACKGROUND:** Advances in detailed representation of disease mechanisms provide new solutions for the development of personalised medicine. Successful projects have built reference computational resources for cancer, Parkinson's disease, Alzheimer's disease and influenza (Kuperstein et al., 2015, PMID 26192618; Fujita et al., 2014, PMID 23832570; Mizuno et al., 2012, PMID 22647208; Matsuoka et al., 2013, PMID 24088197). These are applied for modelling, advanced hypothesis generation and their subsequent validation in relevant clinical contexts (Chanrion et al., 2014, PMID 25295490; Jdey et al., 2016, PMID 27559053; Kuperstein et al., 2015, PMID 25688112).

**OBJECTIVES:** In this work we developed a pathway-based representation of asthma mechanisms using literature, databases, inputs from domain experts, combined with the use of a tool for semi-automatic merging of relevant pathways.

**METHODS:** The overview diagram is designed together by computational biology and asthma domain experts and used to determine the content of the detailed layers. The representation is constructed automatically with a newly developed dedicated pathway merging tool, using the yEd Graph Editor and information from selected MetaCore Pathway Maps converted to the Systems Biology Graphical Notation (SBGN) Activity Flow language (Le Novère et al., 2009, PMID 19668183) for making it both human- and machine-readable.

**RESULTS:** We introduce the AsthmaMap resource (<http://asthma-map.org>), a multiscale representation of asthma mechanisms. It is a collection of interconnected asthma-relevant pathways and networks. The Activity Flow layer (<http://asthma-map.org/af>) consists of 15 cell-specific maps with 2650 nodes and 4716 edges in total and includes 831 unique entities. We discuss the challenges faced in the semi-automatic assembly of such maps. With the proposed technology, the resource becomes highly flexible, less dependent on manual work, and it can be easily updated when new information becomes available.

**CONCLUSION:** In the context of the Disease Maps Community effort (Mazein et al., 2018, in press; Ostaszewski et al., 2018, PMID 29688273) the development of new technological solutions opens promising possibilities for the efficient construction of new disease maps.

While being complementary to other pathway analysis solutions, the AsthmaMap enables 'omics data visualisation and interpretation in the asthma-specific context, thus supporting the process of personalised systems medicine for the understanding and treatment of this complex disease.

AVAILABILITY: All relevant data are available at <http://asthma-map.org>. The code of the merging tool is written in Python and accessible at <https://github.com/eisbm/BioMerger>. The code of the yEd-specific GraphML-SBGN converter is written in Java and available at <https://github.com/eisbm/ySBGN>.

ACKNOWLEDGEMENTS: Funded in part by the Innovative Medicines Initiative (U-BIOPRED n°115010, eTRIKS n°115446).



