

**Thailand** is still one of 22 TB high burden countries. The estimate of new TB cases per year was **117,000** and the estimate number of TB deaths was **13,800** in 2015 (include HIV+). (Global TB report, 2016) **Sustainable development goals (SDGs)** include ending the epidemic of TB for one of health targets. 95% reduction in number of TB deaths and 90% reduction in TB incidence rate by **2035** compared with 2015 is a global target. **Innovative interventions and researches** are urgently required to control TB and achieve the goal.



Our research project has started since 2015 aiming to integrate application of both **human and pathogen genomic information** and **develop new technologies to control TB**. The project is conducted under the Science and Technology Research Partnership for Sustainable Development program (**SATREPS**) in the field of infectious diseases control supported by Japan Agency for Medical Research and Development (**AMED**) and the Japan International Cooperation Agency (**JICA**). The large-scale analysis of both **human and pathogen genomes** revealed how **genome DNA variants** are associated with the development of TB.

## 1 Human genetic risk and biomarker



TB infection is controlled by human immunogenetic factors. **Genome-wide association study (GWAS)** identified specific genetic risk factors for TB. Moreover, **diseases specific gene expression signature** in patient's blood shall help TB diagnosis and monitoring TB

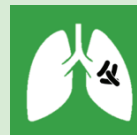
activity. A scoring system (**TB sick score**) combining RNA gene expression signatures supports diagnosis of active TB. (Satproedprai 2015)



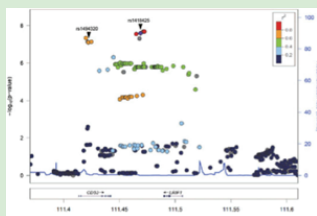
## 2 Mycobacterium Tuberculosis genomic information



The implementation of genotyping based outbreak investigation of **Mycobacterium tuberculosis** will strengthen TB control in Thailand. Whole genome sequencing of *M. tuberculosis* enables precise **monitoring of community transmission and outbreak**, shorten time to **detect second-line drug-resistant tuberculosis**, and reveal genetic factors that may affect unfavorable treatment outcome.



## 3 Interaction between human and pathogen genome variants

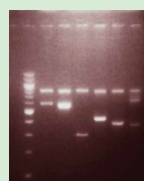


In Thailand, almost half of TB lineage is **Beijing** and the remaining second most common is **East-African Indian (EAI)**. Heterogeneity of pathogen in Thailand makes it possible to analyze **lineage-dependent host genetic factors** in homogenous host genetic background. With this

host-pathogen interaction approach, the specific lineage dependent risk of **CD53** and **HLA class II genes** were identified. Identification of novel host-pathogen interactions are ongoing. (Omae 2017, Toyo-oka 2017)



## 4 Prediction system of treatment response and adverse effects based on genomic information



Most common adverse drug reactions to anti-tuberculosis drug is drug induced **liver injury**. Our human genome analysis in Thailand reinforce the known association between **NAT2 genes** and liver injury. (Wattanapokayakit 2016). According to the results, **NAT2-haplotype specific PCR to predict acetylator type** (rapid, intermediate, or slow) for TB precision medicine was developed. Determination methods of plasma level of first and second line anti-tuberculosis drugs were also developed.



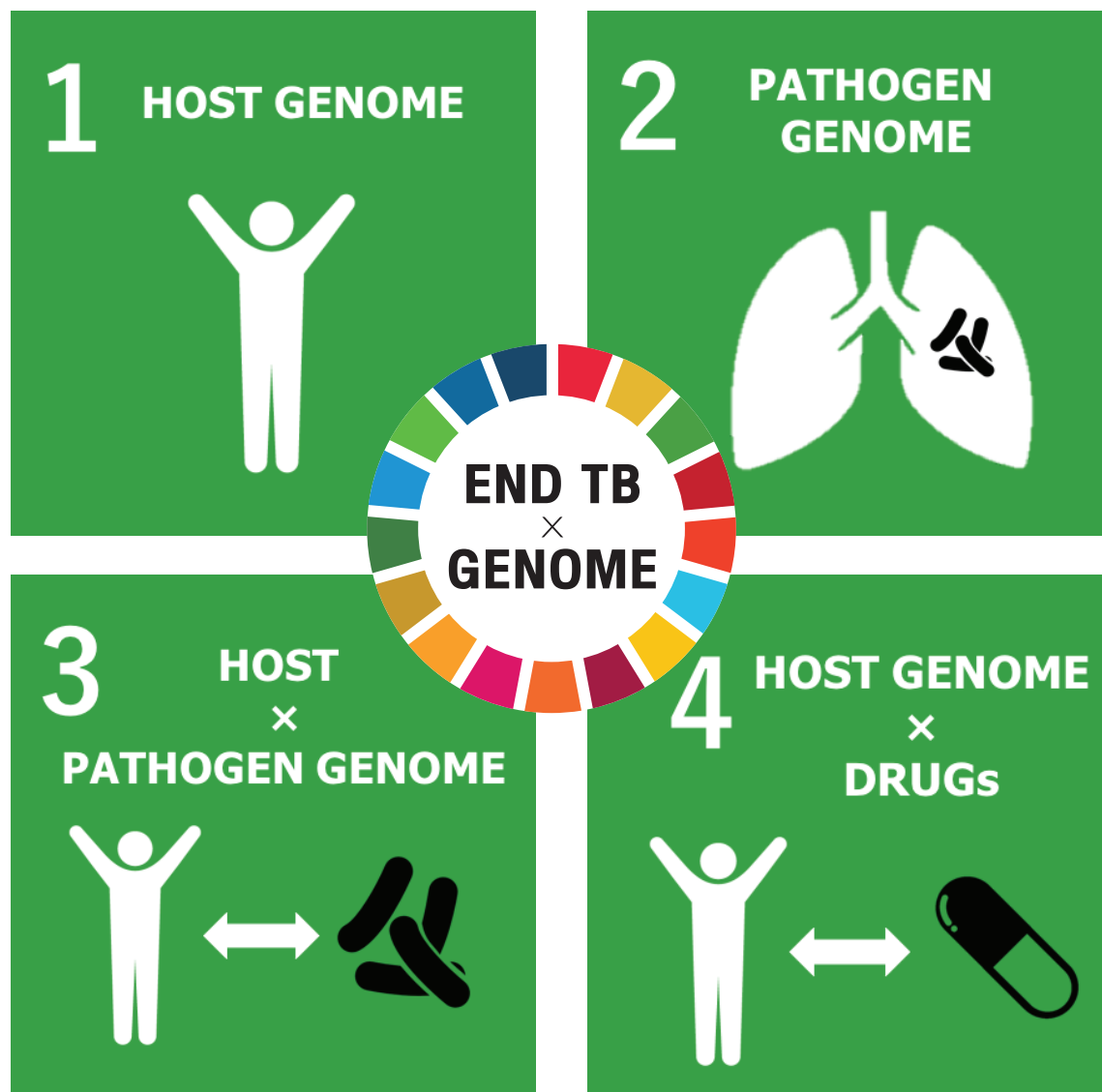
## Publication List

- Omae, Y., Toyo-oka, L., et al. (2017) Journal of Human Genetics, 117, 1-8
- Toyo-Oka, L., S. Mahasirimongkol et al. (2017) HLA, 90 (3), 149-156
- Wattanapokayakit, S., Mushiroda, T. et al. (2016) Int J Tuberc Lung Dis, 20(10), 1364-1369
- Satproedprai, N., Wichunkchinda, N., et al. (2015) Genes Immun, 16 (4), 253-360



# Integrative Application of Human and Pathogen Genomic Information for Tuberculosis Control Project

SATREPS 2015-2019



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