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Deciphering the molecular mechanism of ineffective erythropoiesis in β-thalassemia/Hb E from integrated proteomic analysis

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β-thalassemia/Hb E is a global health issue, characterized by a range of clinical symptoms from a mild and asymptomatic anemia to severe disorders requiring transfusions from infancy. Pathological mechanisms of the disease involve the excess of unmatched alpha-hemoglobin and iron overload leading to an ineffective erythropoiesis and ultimately to the premature death of erythroid precursors in bone marrow (BM) and peripheral organs. However, it is unclear how BM microenvironment factors and hematopoietic stem cells interaction contribute to the defective erythropoiesis in β-thalassemia/Hb E patients. Here, we employed mass spectrometry-based comparative proteomics to analyze BM plasma and $CD34^+$/HSCs protein collected from β-thalassemia/Hb E patients and healthy donors. The differential expressed proteins are enriched from bone marrow plasma derived secretory or exosome-associated proteins, phosphoproteins and intracellular protein from $CD34^+$/HSCs during erythroid development. The constructed protein-protein interaction networks of secretory and intracellular proteins revealed many of which have putative functions in oxidative stress response and associated with the cellular dynamic switching of survival and death pathways. Remarkably, the candidate signaling proteins belongs to PI3K, ubiquitin-proteasome and p53 pathways. Our results highlight that the disease condition of ineffective erythropoiesis and oxidative stress found in BM microenvironment of β-thalassemia/Hb E patients is associated with the impaired intracellular proteins. Moreover, this molecular mechanism from the integrated proteome data is highly possible for further therapeutic approach.

Biography

Saranyoo Ponnikorn had completed his PhD in Biochemistry from Mahidol University Faculty of Science in 2011. He is Lecturer in medical school and member of administrative staff as Assistant to the Dean in academic affairs and medical education from Chulabhorn International College of Medicine, Thammasat University. Moreover, he also works with private companies including Next Generation Genomics and Safe Fertility and PGD Center as Clinical Laboratory Supervisor in genetic diagnosis since 2013. His research is mainly focusing on the signaling pathway of stem cell and disease development such as thalassemia and some skin disorder using proteomic strategies. He is also interested in the application of Thai herbal medicine and drug discovery under *in vitro* stem cell model and developing the feasible and reliable genetic testing for reproductive healthcare.

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