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Reverse Pharmacology for developing Novel Compounds for Malaria

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Malaria as VBD is of crucial medical importance within context of raising resistance and lack of new alternatives. There are challenges of R&D pharma for new drugs, potential to use reverse pharmacology for new compound evaluation. Reverse pharmacology is the science of integrating documented clinical/experiential hits, into leads by transdisciplinary exploratory studies and further developing these into drug candidates by experimental and clinical research. Many potential compounds seems to be used in traditional medicine in Asia and Africa which share many similarities and this effort seems to be confirmed by agreement between Malaysia and India to move forward this direction (only one of many examples) The scope of reverse pharmacology is to understand the mechanisms of action at multiple levels of biological organization and to optimize safety, efficacy and acceptability of the leads in natural products, based on relevant science. Latest anti-malarial drugs Artemisinin derivatives & ACTs are becoming ineffective in malaria endemic countries (Dr Charlie Woodrow et al. Lancet, Feb.2015, D L Saunders, The Infectious Diseases, Lancet, June 2015). Accurate diagnostic and surveillance with better understanding of genetic and immunologic background of host specific response and pathogen evolution drives adapted research but also preventive interventions.

As one of examples to illustrate it, global mapping of resistance to artemisinin (the KARMA study driven by Institut Pasteur in Paris and the Institut Pasteur in Cambodia and members of Institut Pasteur International Network) monitoring risk of spread of artemisine resistance from Asia to Africa using discovery of kelch(K13)-propeller domains as the primary determinant of artemisinin resistance. In an observational cohort study, a herbal drug has been tried in 35 cases of Drug Resistant Malaria in children of 5 to 8 year's age, during Feb 2014 to June 2016, in India. Only patients showing resistance to Chloroquine & Artemether + Lumefantrine combination therapy (ACT) were included for study. Every patient was given 3 days' indoor treatment with herbal drug. Pulse Rate & Temperature was monitored 6 hourly. Blood smear for parasite was examined at 12 hours, 24 hours, 30 hours, Day-5, Day-30 & Day-60. Fever Clearance Time observed was 30 to 48 hours in 98% cases of *P. falciparum* & 94% cases of *P. vivax*. Parasite Clearance Time observed was 12 to 30 hours in about 98% cases of *P. falciparum* & about 94% cases of *P. vivax*. None of the successfully treated patients got recurrence in next 8 months' time. There was no intolerance / adverse reaction to the herbal drug. Concept of Immuno-Modulation applied to herbal anti-malarial drug, can explore potential for discovery of novel herbal drug for Neglected Tropical Diseases also.