

Prehistory and Health. What Anthropological and Linguistic Data Tell Us about the Global Distribution of Hyperreactive Malarial Splenomegaly

Hyperreactive Malarial Splenomegaly [HMS]



A syndrome marked by persistent splenomegaly, exceptionally high levels of malaria antibody, and hepatic sinusoidal lymphocytosis, possibly caused by a disturbance in T cell control of the humoral response to recurrent malaria.

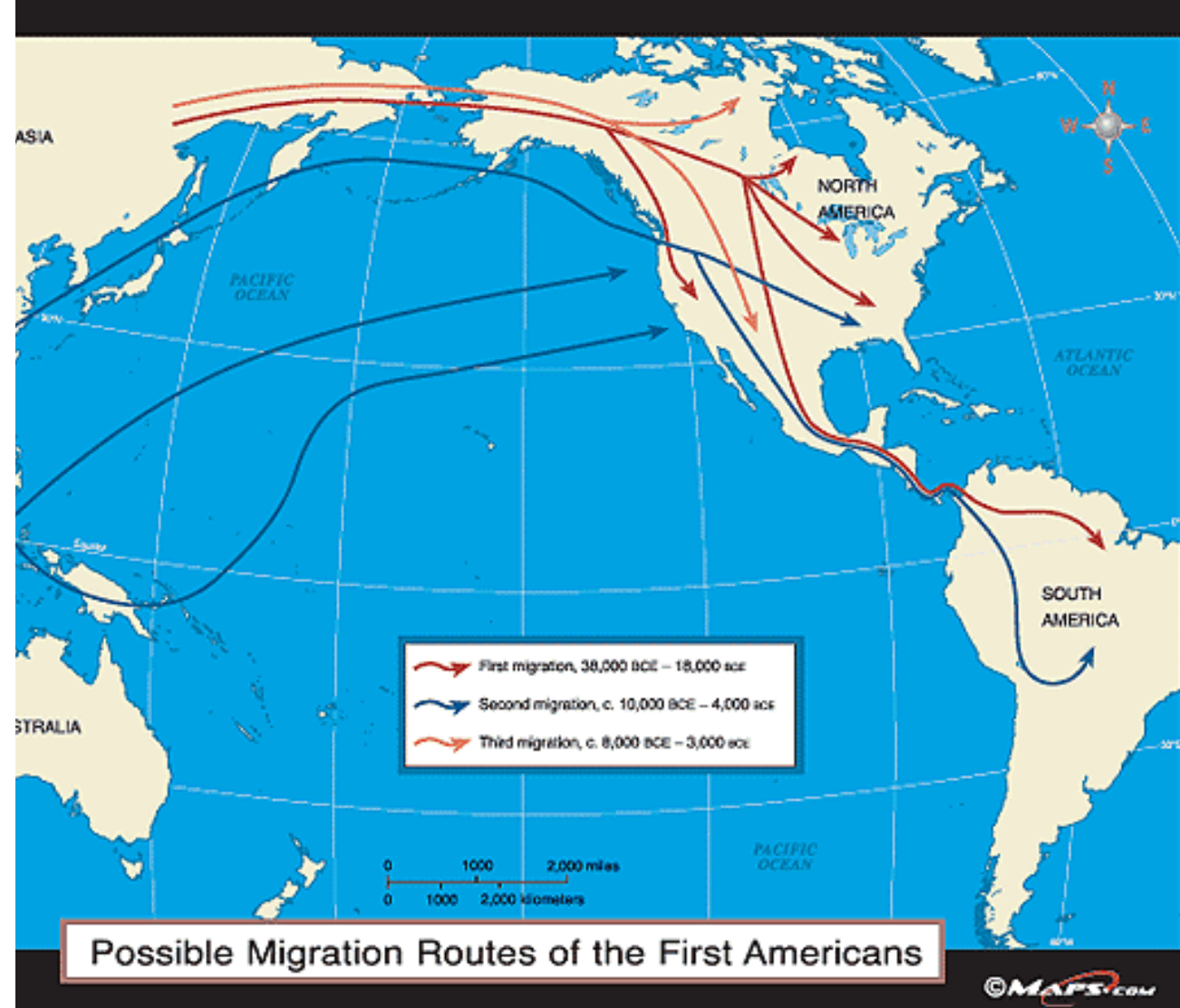
- Elevated serum IgM is recognized as the most important feature of the disorder—the remaining clinical signs are sequelae.
- In HMS, IgM constitutes a substantial proportion of the individual's antimalarial antibodies though only a small proportion of it has been found to be antimalarial.
- The remaining IgM is autoantibodies with specificity for altered IgG and other autoantigens.

Epidemiology

- Formerly known as tropical splenomegaly syndrome [TSS], HMS is an aberrant response to chronic malarial infection.
- HMS is associated with high mortality (50% five year mortality in Papua New Guinea and Uganda) among untreated patients; infection being the leading cause of death.
- The incidence of HMS is highest among the people of the Upper Watut Valley in Papua New Guinea, where the rate is estimated to be 80%.
- Given the populational and familial patterns of this disorder, an as-yet-undefined genetic predisposition is suspected.

Malaria and HMS in the New World. Archaeo-epidemiological Evidence

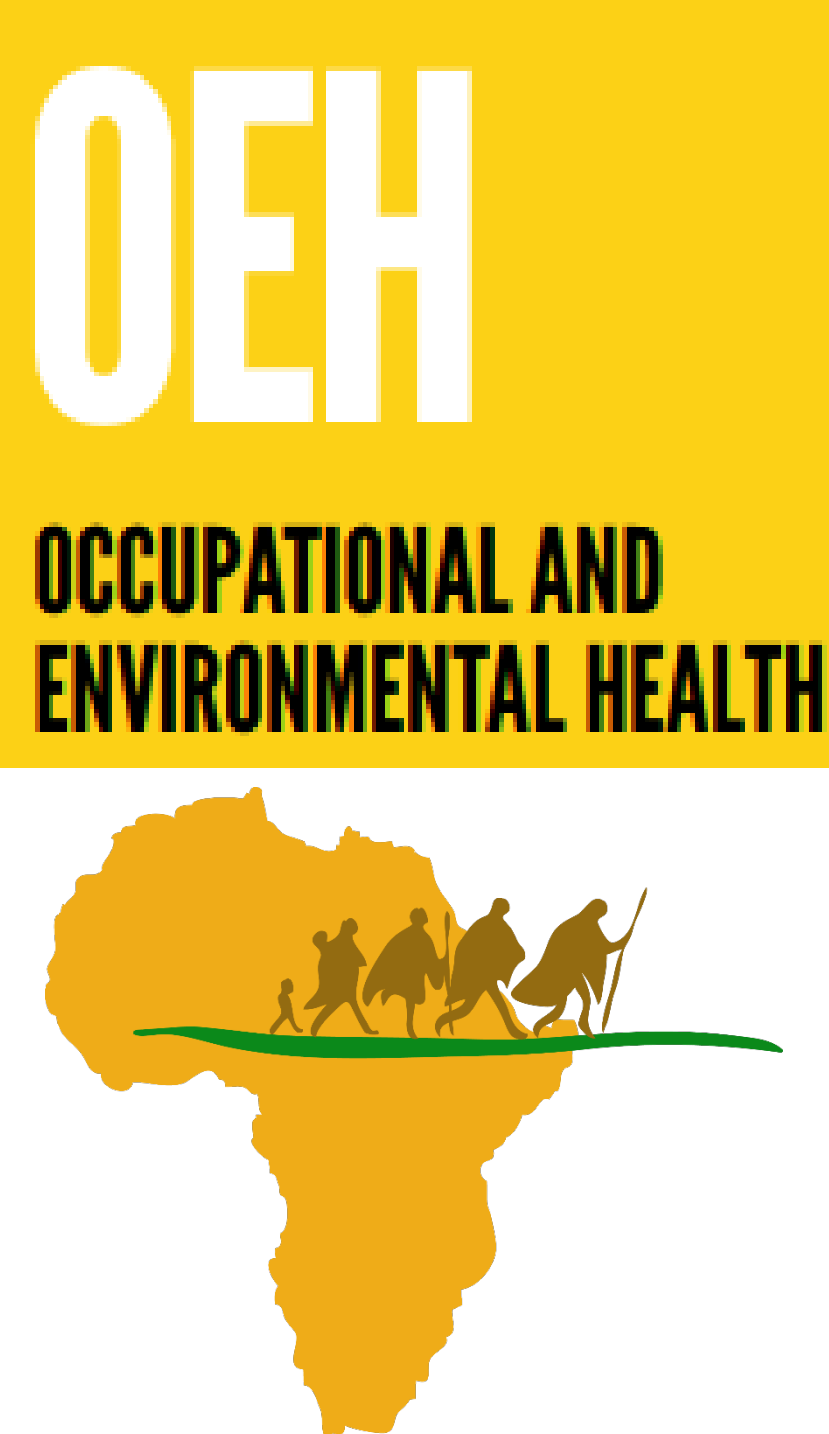
"A... seroepidemiological survey seeking hyperreactive malarial splenomegaly was carried out in isolated Yanomami hamlets in Amazonas Territory in Venezuela. All 110 inhabitants greater than 1 year of age were evaluated... The spleen index for individuals greater than 10 years of age was 44%. ...Twenty-three patients were considered to show hyperreactive malarial splenomegaly. Clinical manifestations of the syndrome did not differ from those described in other parts of the world." (Torres et al. 1988)



Gm^{za}::g

Gm^{fa}::b*

Contrast



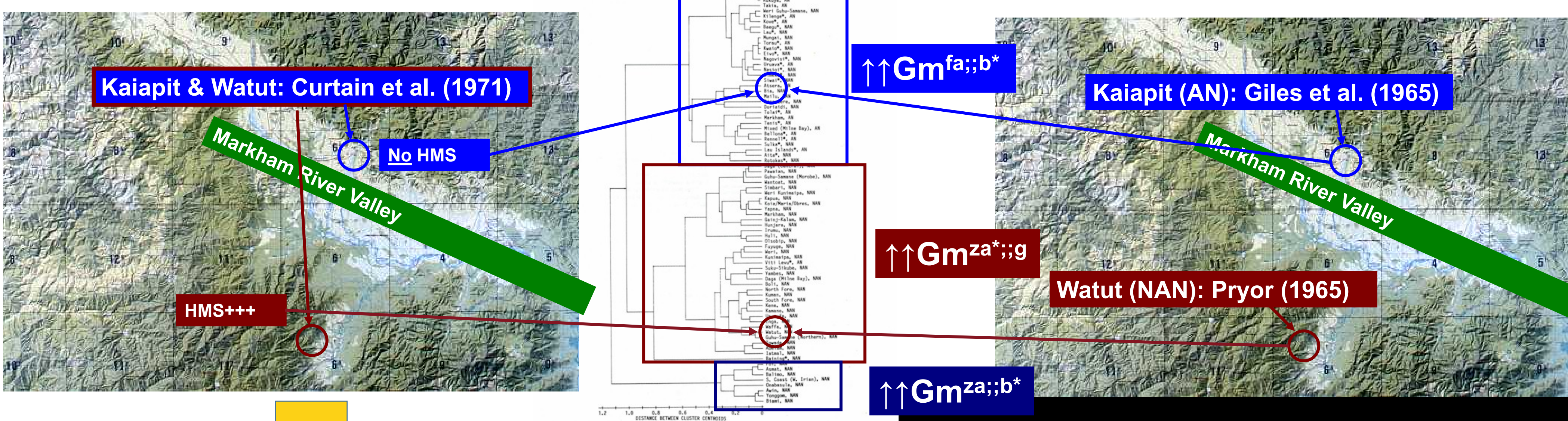
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Background

We describe how anthropological and linguistic data can be used to inform hypotheses about the genetic basis of HMS and to identify indigenous populations at health risk globally.

The example described here illustrates how seemingly disparate intellectual pursuit [in this case, 1) explaining the origins of the Polynesian peoples and 2) identifying the genetic basis of hyperreactive malaria splenomegaly] may converge to illuminate both problems.

Prehistory and Health



- ✓ Deadly fevers - probably malaria - have been recorded since the beginning of the written word (6000-5500 B.C.) References can be found in the classic Chinese medical text, Nei Ching (4650 B.P), Vedic writings (3500 B.P) and by Hippocrates some 2500 years ago.
- ✓ There are no references to malaria in the "medical texts" of the Mayans or Aztecs. It is likely that European settlers and slavery brought malaria to the New World and the awaiting anophelines within the last 500 years.

Conclusions

- Anthropological, archaeological and linguistic data related to populations at-risk or resistant to HMS suggest that genetic susceptibility to HMS arises from antigenic IgG variations.
- At the same time, the resistance of Austronesian-speaking peoples indicates an evolutionary advantage that allowed them to enter and settle coastal Melanesia and eventually Polynesia.

Global events such as deforestation, environmental degradation and climate change threaten more and more historically unexposed indigenous populations to malaria.

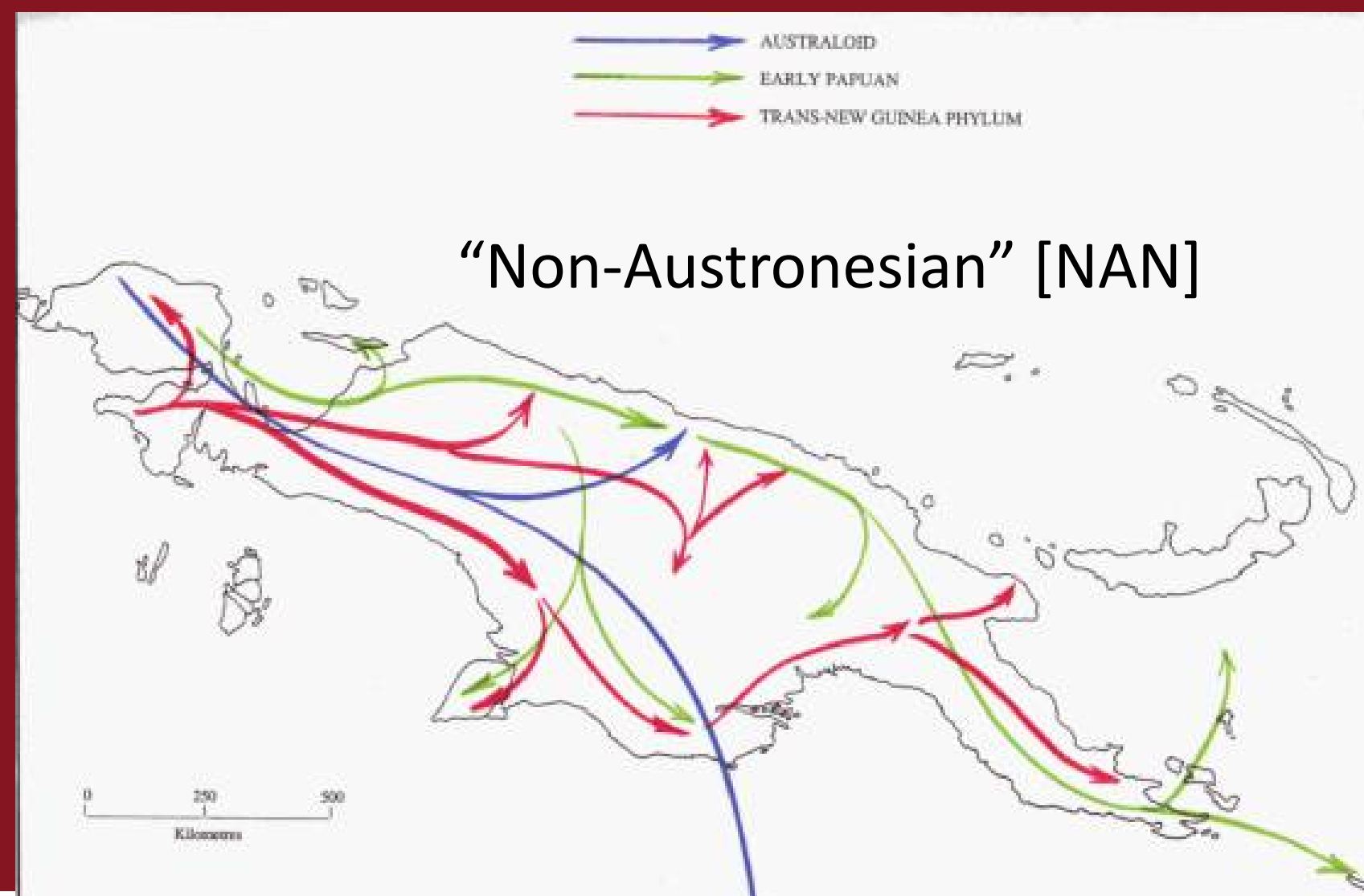
Gm Correlations with Altitude as a Surrogate for Malaria

Rank-Order Correlations of Gm Haplotypes and Alleles with Altitude

Populations and Haplotypes or Alleles		IgG Antigenic Polymorphisms		
	N	Correlation	p	
Markham Valley	25			
Gm ^{fa} ::b*		0.490	< 0.001	
Gm ^{ak} ::g		0.410	< 0.05	
Gm ^{ai} ::b		-0.509	< 0.001	
New Guinea	42			
Gm ^{fa} ::b*		0.531	< 0.001	
Gm ^{ak} ::g		0.362	< 0.01	
Gm ^{ai} ::b		-0.178	n.s.	
Gm ^{fa} ::b		-0.214	n.s.	
Gm ^{ak} ::g		0.189	n.s.	
Gm ^{ai} ::b		0.362	< 0.01	
Gm ^{ak} ::g		0.178	n.s.	
Gm ^{ai} ::b		0.536	< 0.001	
Gm ^{ak} ::g		-0.544	< 0.001	
Island Melanesia				
Gm ^{fa} ::b*		-0.026	n.s.	
Gm ^{ak} ::g		0.074	n.s.	
Gm ^{ai} ::b		-0.252	n.s.	
Gm ^{fa} ::b		0.066	n.s.	
Gm ^{ak} ::g		-0.061	n.s.	
Gm ^{ai} ::b		0.074	n.s.	
Gm ^{ak} ::g		0.066	n.s.	
Gm ^{ai} ::b		-0.035	n.s.	
Gm ^{ak} ::g		0.013	n.s.	

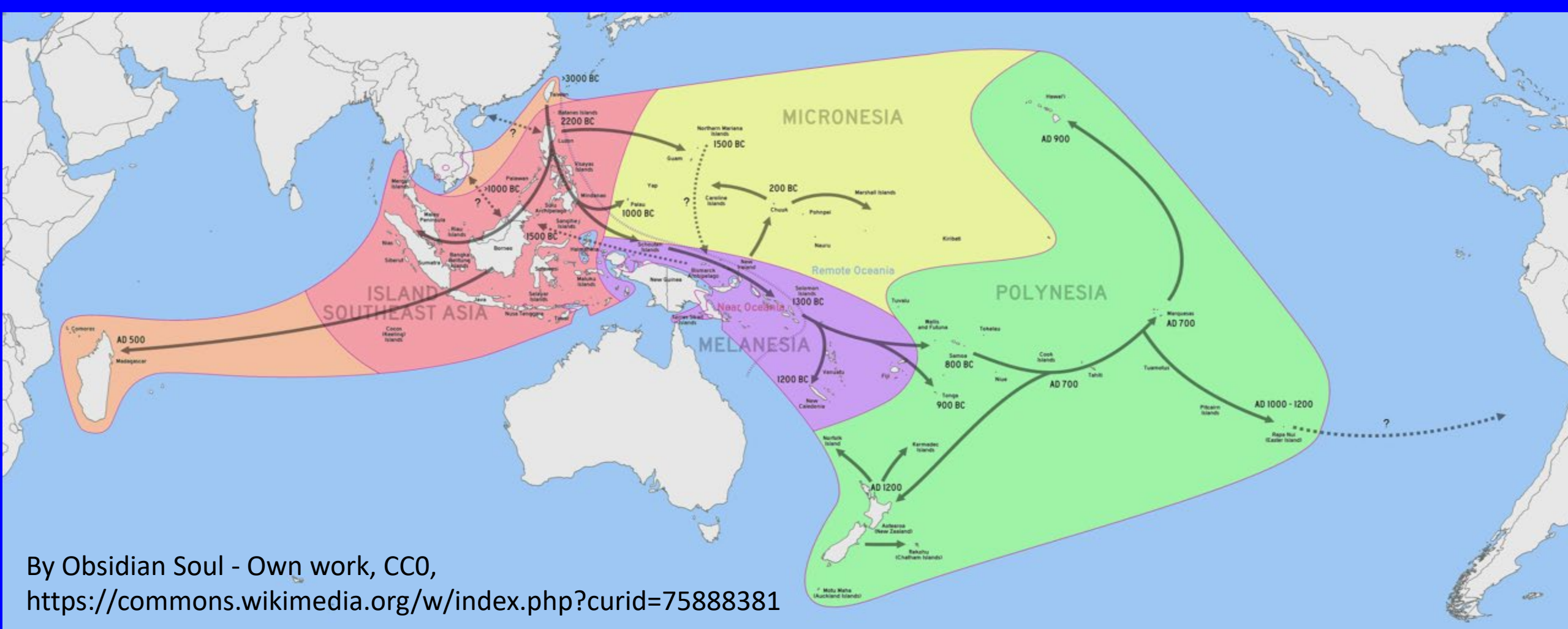
Early Settlement of the Pacific

- The Pacific Islands were first settle 60,000 ybp ago by the peoples who colonized Australia.
- The highlands of New Guinea (pictured to the right) were inhabited around 50,000 ybp.



Horticulture developed in the New Guinea highlands around the same time as in other areas of the world.

"Austronesian" Expansion



Three competing theories of the spread of humans into Polynesia—each attempting to explain how the Polynesians migrated through or developed out of the long-established Non-Austronesian speaking peoples of Melanesia:

- Express Train model: A recent (c. 3000–1000 BCE) expansion out of Taiwan
- Entangled Bank model: Emphasizes the long history of Austronesian speakers' cultural and genetic interactions with indigenous Island Southeast Asians and Melanesians.
- Slow Boat model: Similar to the express-train model but with a longer hiatus in Melanesia along with admixture

Resources

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