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Molecular Medicine Communications

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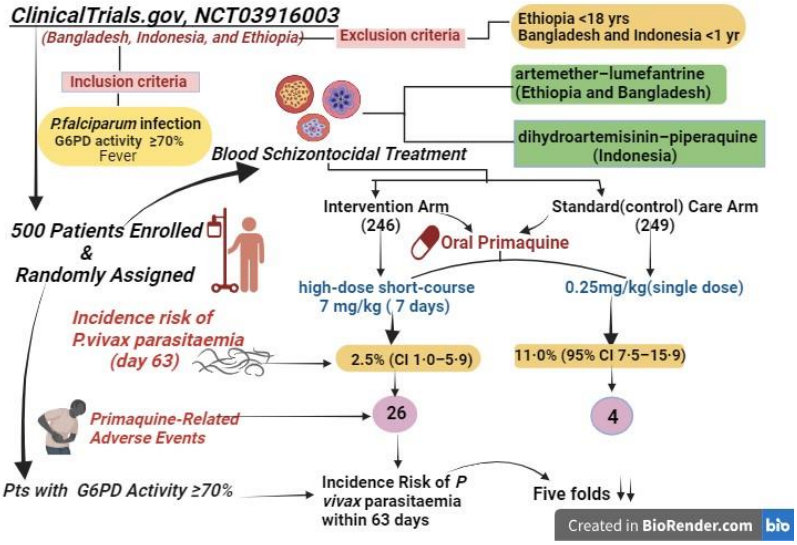
Editor's Choice

Editor's Selection of the Important Research Investigations in the Field of Molecular Medicine Communications from Around the World

Editorial Staff

Primaquine Reduces *P vivax* Parasitemia Risk

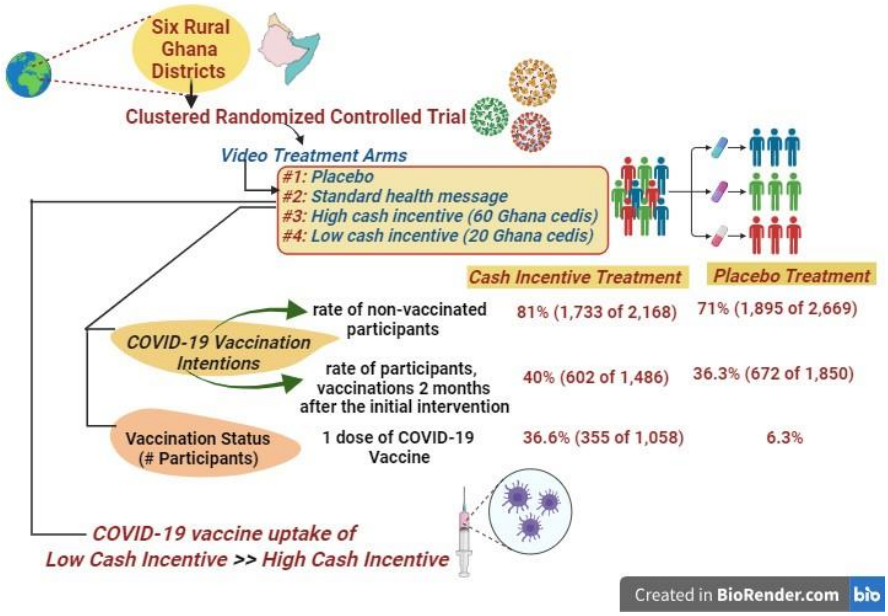
In areas where both P falciparum and P *vivax* are co-endemic, and a patient is diagnosed with P falciparum malaria, the standard practice is to treat the acute infection with an appropriate antimalarial, often an Artemisinin-based combination therapy (ACT). Primaquine is not typically used for treating the acute P falciparum infection. However, adding primaquine to ACT could help reduce their risk of subsequent *P vivax* parasitemia. Thriemer and colleagues performed a multicenter clinical trial across Bangladesh, Indonesia, and Ethiopia. The primary endpoint was the incidence risk of *P vivax* parasitemia on day 63. This trial was registered at ClinicalTrials.gov, NCT03916003. The trial recruited 500 patients and the results suggest that there were very few serious adverse effects while 143 mild adverse effects were also reported. The incidence risk of *P vivax* parasitemia at day 63 was 11·0% (95% CI 7·5–15·9) in the standard care arm (low dose primaquine) compared with 2·5% (1·0–5·9) in the intervention (high dose primaquine) arm (hazard ratio 0·20, 95% CI 0·08–0·51; p=0·0009). These results suggest that high-dose short-course primaquine can reduce *P vivax* parasitemia risk within 63 days by fivefold. Lancet. 2023 Dec 2;402(10417):2101-2110. doi: 10.1016/S0140-6736(23)01553-2.



Financial Incentives for COVID-19 Vaccines Help

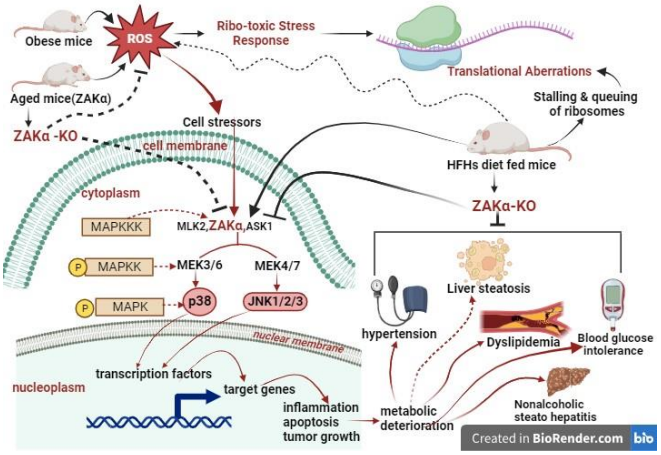
Cash incentives for COVID-19 vaccination involve offering individuals a financial reward as an encouragement to get vaccinated against the coronavirus. This strategy has been implemented by various governments, organizations, and businesses as part of their efforts to increase vaccination rates. Duch and colleagues randomly assigned about 700 residents of several villages in Ghana to four groups in a cluster-controlled trial. The results show that

participants assigned to the cash incentive treatments had an average rate of 81% (1,733 of 2,168) compared to 71% (1,895 of 2,669) for those in the placebo treatment arm. For self-reported vaccinations, the average rate for participants in the cash treatment was 3.5% higher than for participants in the placebo treatment (95% confidence interval (CI): 0.001, 6.9; $P = 0.045$): 40% (602 of 1,486) versus 36.3% (672 of 1,850). These results suggest that cash incentives help in vaccination uptake but paradoxically, low cash incentives resulted in higher vaccine uptake compared to high cash incentives. We found that cash incentives motivate individuals who may be hesitant or reluctant to receive the COVID-19 vaccine. Financial rewards can serve as an additional motivator for those who may be on the fence about getting vaccinated. Trial identifier: AEARCTR-0008775. Nat Med. 2023 Nov 27. doi: 10.1038/s41591-023-02670-4.



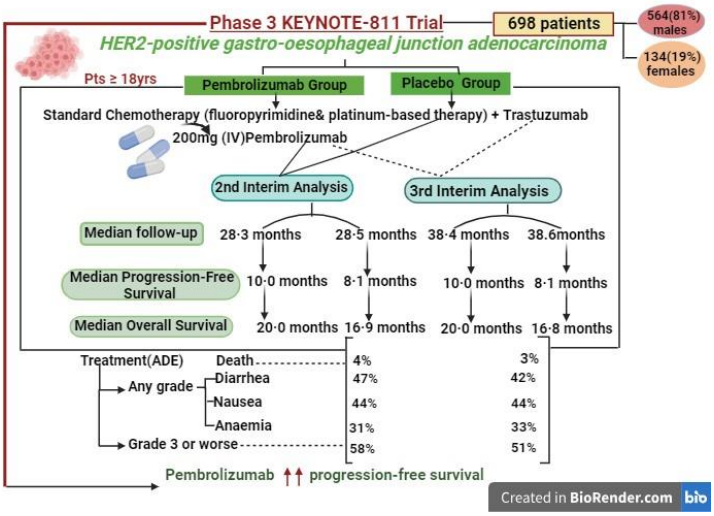
Role of ZAKα-Mediated Metabolic Decline in Obesity and Aging

It has been known that there exists a connection between oxidative stress, ribosomal dysfunction, and the metabolic decline observed in conditions such as obesity and aging. The ribotoxic stress response (RSR) is a signaling pathway in which the p38- and ZAKα sense stalling and/or collision of ribosomes. ZAKα, also known as MAP3K20, is a mitogen-activated protein kinase kinase kinase (MAP3K) that plays a role in cellular signaling pathways. Snieckute and colleagues show that reactive oxygen species (ROS)-generating agents trigger ribosomal impairment and ZAKα activation. They also found that ZAK-knockout mice are protected from developing high-fat high-sugar (HFHS) diet-induced blood glucose intolerance and liver steatosis, stressing the role of the RSR in metabolic regulation. Their study revealed the hallmarks of metabolic aging in animals after ZAK ablation. Understanding these molecular pathways could provide insights into the cellular mechanisms contributing to metabolic dysfunction in these conditions and may potentially lead to the development of targeted interventions or therapies. Science 2023 Dec 8;382(6675):eadf3208. doi: 10.1126/science.adf3208.



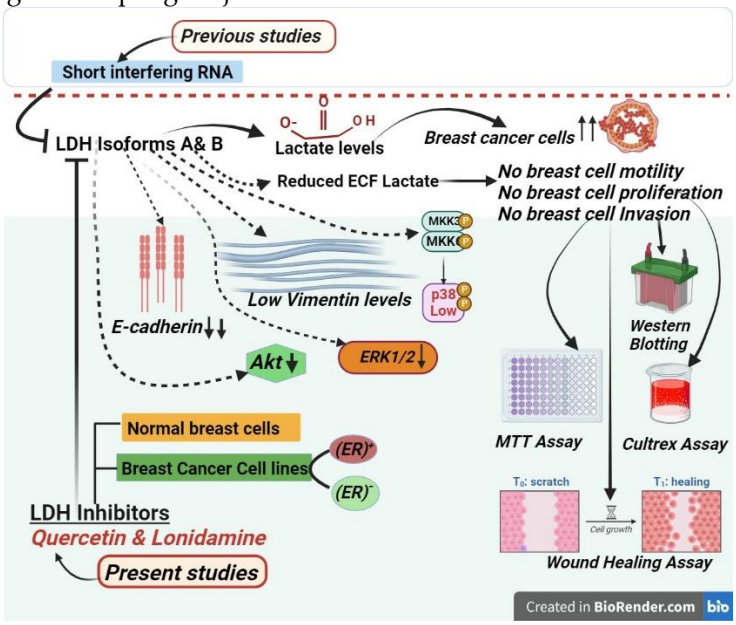
A New Role for Lactate in Breast Cancer

Lactate dehydrogenase (LDH) is an enzyme that plays a key role in cellular metabolism by converting pyruvate to lactate during anaerobic glycolysis. LDH has been implicated in various cancer types, including breast cancer, where increased LDH activity is associated with tumor growth, invasion, and resistance to therapy. LDH inhibitors are being investigated as potential therapeutic agents in cancer treatment, including breast cancer. Khajah and colleagues investigated the role of LDH inhibitors in both estrogen receptor $(ER)^+$ and ER^- breast cancer cell lines and in normal breast epithelial cells. A significant reduction in extracellular lactate level, cell proliferation, motility, and invasion was observed after treatment with LDH inhibitors. Subsequently, changes in the levels of vimentin, E-cadherin, p38 MAPK, ERK1/2, and AKT were also observed. Cancer cell proliferation was preferentially blocked compared with normal epithelial cell inhibition by LDH inhibitors such as quercetin and lonidamine. These results further highlight the role of lactate in breast cancer progression and indicate the practical use of various commercially available LDH inhibitors as promising therapeutic agents to oppose the processes leading to cancer progression. While LDH inhibitors show promise, challenges include achieving selectivity for cancer cells and minimizing toxicity to normal tissues. The development of specific LDH inhibitors with favorable pharmacokinetic properties is an ongoing area of research. Mol Med Rep. 2024 Jan;29(1):12. doi: 10.3892/mmr.2023.1313.



Pembrolizumab Plus Trastuzumab and Chemotherapy for HER2-Positive Gastric or Gastro-oesophageal Junction Adenocarcinoma

The combination of pembrolizumab, and trastuzumab chemotherapy has long been investigated in the treatment of HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma. HER2-positive gastric or gastroesophageal junction adenocarcinoma refers to cancers that overexpress the human epidermal growth factor receptor 2 (HER2), which is associated with more aggressive tumor behavior. Pembrolizumab is a monoclonal antibody that targets the programmed cell death protein 1 (PD-1) receptor, a checkpoint protein on immune cells.



By blocking PD-1, pembrolizumab helps unleash the immune system to target and attack cancer cells. Trastuzumab is another monoclonal antibody that specifically targets HER2-positive cancer cells. It has been a standard treatment for HER2-positive breast cancer and has been explored in HER2-positive gastric and gastroesophageal junction cancers. Janjigian and colleagues revealed the interim analysis of a randomized, phase 3 KEYNOTE-811 trial which involved 168 medical centers in 20 countries worldwide. They found that compared with placebo, pembrolizumab significantly improved progression-free survival when combined with first-line trastuzumab and chemotherapy for metastatic HER2-positive gastro-oesophageal cancer, specifically in patients with tumors with a PD-L1 combined positive score of 1 or more. They stated that the overall survival follow-up is ongoing and will be reported at the final analysis. Lancet. 2023 Dec 9;402(10418):2197-2208. doi: 10.1016/S0140-6736(23)02033-0.

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