expression (2.65 to 7.1 fold in TLR2 and 3.72 to 3.31 fold for TLR9). In addition, pro-inflammatory cytokine responses, including IL-1b, TNF-a, IL-6, IL-12p70 and IFN-g, to TLR2 and 9 ligands are significantly diminished in filarial-TB coinfected individuals compared to individuals with latent TB alone. Pro-inflammatory cytokine production in response to TLR4 ligand stimulation (used as a control TLR stimulus) is not altered in co-infected individuals. Definitive treatment of lymphatic filariasis significantly restores the pro-inflammatory cytokine responses in individuals with latent TB (ranging from a 2 to 10 fold increase for the different cytokines) at one year post antifilarial therapy. Thus, coincident filarial infection exerted a profound inhibitory effect on protective mycobacteria specific TLR mediated immune responses in latent tuberculosis and suggests a novel mechanism by which concomitant filarial (and other systemic helminth) infections could predispose to the development of active tuberculosis in humans.

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HELMINTH-MEDIATED PROTECTION AGAINST AUTOIMMUNE DIABETES IN NOD MICE IS NOT DEPENDENT ON A TH2 IMMUNE SHIFT

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A broad range of helminths have been shown to have beneficial effects on autoimmune diseases. A leading hypothesis to explain this phenomenon is that helminth-induced type 2 immune responses limit pathogenic Th1-driven autoimmune responses. To investigate this hypothesis, the effects of *Litomosoides sigmodontis* infection on the development of Type I diabetes was evaluated in IL-4$^{-/-}$ nonobese diabetic (NOD) mice and compared with immunocompetent (WT) NOD mice. Infection of WT NOD mice with the filarial nematode *L. sigmodontis* prevented the onset of diabetes and was associated with a Th2 shift in cytokine production with significantly increased amounts of IL-4 and IL-5 from anti-CD3/anti-CD28 stimulated spleen and pancreatic lymph node cells. Significantly increased production of insulin-specific IgG1, but not insulin-specific IgG2c, showed that this Th2 shift was also present in response to one of the main autoantigens in diabetes. In contrast, IL-4$^{-/-}$ NOD mice failed to develop a Th2 shift during *L. sigmodontis* infection. Compared to WT mice, IL-4$^{-/-}$ NOD mice did not develop detectable IgE during infection, had decreased levels of insulin-specific IgG1 ($p<0.05$), and increased levels of insulin-specific IgG2c ($p<0.001$), suggesting a Th1 shift in response to insulin. In addition, infection of IL-4$^{-/-}$ NOD mice resulted in no increase in splenocyte production of IL-5 or IL-13 compared to uninfected IL-4$^{-/-}$ NOD mice and in significantly lower concentrations compared to infected WT NOD mice. As expected, splenic and pancreatic lymph node IFNγ concentrations were higher in IL-4$^{-/-}$ NOD mice compared to both infected and uninfected WT NOD mice. Interestingly, numbers of splenic CD4^{+} CD25^{+}FoxP3^{+} cells were increased in both WT and IL-4$^{-/-}$ infected mice. Despite the absence of a Th2 shift, infection of IL-4$^{-/-}$ NOD mice with *L. sigmodontis* prevented the onset of diabetes in all mice studied (n=11) whereas uninfected IL-4$^{-/-}$ controls (n=33) developed diabetes at comparable rates (67% at week 24) as WT NOD mice (n=26, 85% at week 24). These studies demonstrate that infections with filarial worms can protect against the onset of Type 1 diabetes in NOD mice by a mechanism that is independent of the host's ability to induce a Th2 shift, possibly through induction of immunoregulatory mechanisms. These results suggest it may be possible to develop worm-derived therapies for autoimmune diseases which do not induce pro-allergic Th2 responses.

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INDOOR USE OF CARBAMATE TREATED PLASTIC SHEETING IN COMBINATION WITH LONG LASTING INSECTICIDAL NETS TO CONTROL PYRETHROID RESISTANT MALARIA VECTORS IN WEST AFRICA

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Recent findings in Benin showed that pyrethroid resistance in *Anopheles gambiae* can reduce the efficacy of insecticide treated nets (ITN) and indoor residual spraying (IRS) recommended for malaria vector control. In this context, we have tested a new strategy based on a combination of long lasting insecticidal net (LLIN) and carbamate treated plastic sheeting (ITPS) to improve personal protection and "killing effect" against pyrethroid resistant mosquitoes. Experimental huts trial according to WHO phase II procedures was carried out in "Vallée du Kou" (Burkina Faso) where *An. gambiae* M and S molecular forms are sympatric and exhibit high level of pyrethroid resistance. Efficacy of LLIN (PermaNet® 2.0) alone and either in combination with ITPS (bendiocarb, 400 mg/m²), or in combination with IRS (bendiocarb, 400mg/m²) were compared in phase II trial. 1,374 *An. gambiae* were collected during the 2 months of evaluation. The blood feed inhibition was 43.4%, 58.1%, 56.3% with LLIN, LLIN+ITPS and LLIN+IRS respectively, suggesting that LLIN remains effective in term of personal protection against pyrethroid resistant mosquitoes. Low mortality rates were observed with the LLIN (44.0%), IRS (42.4%) and ITPS (52.5%) whereas both combinations killed significantly more mosquitoes (72.6% and 66.4% for LLIN+ITPS and LLIN+IRS). The results suggested that the association LLIN+ITPS (or LLIN+IRS) is a promising alternative to control pyrethroid resistant mosquitoes. A phase III trial is currently evaluating this strategy at community level in Benin to assess the people acceptability and the efficacy of these combinations on entomological, parasitological and clinical parameters of malaria.

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MULTIPLE INSECTICIDE RESISTANCE AMONG *ANOPHELES GAMBIAE* IN URBAN AGRICULTURAL AREAS OF COTONOU, BENIN (WEST AFRICA)

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Current vector control strategies rely on insecticide-treated nets (ITNs) and indoor residual spraying (IRS). However, the development of insecticide resistance constitutes a major threat to both ITN- and IRS-based control programs. Rapid urbanization without proper roads or drainage systems for rainwater, plus intensive agriculture practices, such as market-gardening, provide favorable conditions for the development of *Anopheles* mosquitoes and urban malaria. The objective of this study was to assess the status of insecticide resistance among *An. gambiae* sl populations in Cotonou, the growing economic capital of Benin. *Anopheles* breeding sites were sampled in urban areas, including market-garden zones, at the end of the dry season and the beginning of the rainy season in 2008. Larvae were brought back to the insectary and reared to adulthood. Bioassays with WHO diagnostic test kits were performed using pyrethroid, carbamate, organophosphate and organochlorine insecticides. *An. gambiae* mosquitoes were identified to species and to M or S molecular forms using PCR. Molecular and biochemical assays were performed to identify Leu-Phe *kdr* and *ace-1R* mutations in individual mosquitoes and to detect increases in the activity of enzymes typically involved in insecticide resistance (oxidases, esterases, glutathione-S-transferases). All