Low doses of diarrhoeagenic E. coli induce enhanced monocyte and mDC responses, and prevent against re-infection in a human challenge model

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A human challenge model was developed to study nutritional interventions to prevent infection with diarrhoeagenic *Escherichia coli*, one of the major and most common causes of diarrhea. Challenges with high doses of *E. coli* was shown to prevent clinical symptoms upon re-infection. Here we aimed to study if a low dose primary *E. coli* challenge induced only partial protection against re-infection. Thirty healthy male volunteers were selected, randomized, and orally exposed to increasing concentrations of *E. coli* strain E1392/75-2A (10e6, 10e7, 10e8, 10e9, and 10e10 CFU). Clinical symptoms of gastrointestinal discomfort were recorded, and stool and blood samples were collected. These were analyzed for immunological responses, stool characteristics, and inflammatory markers. After primary infection, *E. coli*-specific serum IgG(CFA/II) titers increased in a dose-dependent manner. Three weeks later, all volunteers were re-infected with a high *E. coli* dose(10e10 CFU). Surprisingly, all primary *E. coli* doses protected largely against clinical symptoms upon re-infection, with no significant dose-dependency. The only significant dose-dependent effect was a stronger increase in %fecal wet weight after *E. coli* re-infection in the subjects that received a lower dose at primary infection. Additionally, *in vitro* stimulation with *E. coli* resulted in increased numbers of IL-6+/TNF-a+ monocytes and mDC compared to before the primary infection, but this was not dose-dependent. In conclusion, *E. coli* infection with as few as 10e6 bacteria largely protected against re-infection. Although a dose-dependent increase of the IgG response to *E. coli* was observed after primary infection, and a dose-dependent decrease in the change in %fecal wet weight, the IgG response did not directly correlate with clinical protection at secondary infection. The enhanced mDC and monocyte response after primary infection, even though not dependent on *E. coli* dose, indicates that *E. coli* infection induces innate memory to bacterial infection.