

## Monoclonal Antibodies For Biomonitoring Exposure To Methylene Diphenyl Diisocyanate (mdi) Used In Spray Polyurethane Foam Insulation

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**RATIONALE:** Methylene diphenyl and other diisocyanates are a leading cause of occupational asthma world-wide. Exposure is the best recognized risk factor for the development of methylene diphenyl diisocyanate (MDI) asthma, however, current methods for monitoring exposure are limited and better approaches may help prevent new cases. We hypothesize that serologic assays could be developed for biomonitoring MDI exposure, and evaluated the sensitivity of enzyme-linked immunosorbant assays (ELISAs) based on MDI-specific monoclonal antibodies (mAb), for detecting MDI-conjugated human albumin (a biomarker of exposure) in human serum.

**METHODS:** Hybridomas were generated from Balb/C mice that had been immunized with autologous serum proteins reacted with MDI in vitro. Hybridoma supernatants were screened by ELISA for the presence of mouse IgG that bound MDI conjugated human albumin, but not "mock" exposed albumin. A "sandwich ELISA" was subsequently developed using anti-MDI mAbs as capture reagents, and biotinylated goat anti-human albumin as a detection reagent, to quantitate the amount of MDI-albumin in human serum.

**RESULTS:** Six different murine hybridomas that secrete MDI-specific mAbs were produced, and stable, high secreting (>3 µg/ml culture supernatant) subclones were identified. All six mAbs were of the IgG1 isotype/subclass. Following purification, differences in the relative affinities of the mAbs was determined through competitive binding assays, and suggested differences in epitope recognition. Sandwich ELISAs, incorporating the anti-MDI mAbs as capture reagents, were capable of detecting less than 10 ng/ml of synthetic MDI-albumin (prepared in vitro), when spiked into diluted (1:10) human serum.

**CONCLUSIONS:** A highly sensitive ELISA, based on new anti-MDI mAbs, was developed for measuring biomarkers of MDI exposure. The new mAb-based assay may provide a novel approach for monitoring workers' MDI exposure.

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