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**Characterization of amoxicillin and clavulanic acid specific T-cell clones from amoxicillin-clavulanic acid hypersensitivity patients (max 12 words)**

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**Table E1.** Diagnostic evaluation of hypersensitivity patients included in the study.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ID** | **Clinical diagnosis** | **Skin test** | | | | **Drug provocation test** | | |
| **PPL** | **MD** | **AX** | **Clav** | **PV** | **AX** | **AX-Clav** |
| P1 | BL hypers | - | - | **+ (IDT)** | - | **+** | ND | ND |
| P2 | AX hypers | - | - | **+ (IDT)** | - | - | ND | ND |
| P3 | AX hypers | - | - | **+ (IDT)** | - | - | ND | ND |
| P4 | AX hypers | - | - | **+ (SPT)** | - | - | ND | ND |
| P5 | Clav hypers | - | - | - | **+ (IDT)** | ND | - | ND |
| P6 | Clav hypers | - | - | - | **+ (IDT)** | ND | - | ND |
| P7 | Clav hypers | - | - | - | **+ (IDT)** | ND | - | ND |

AX: amoxicillin; BL: betalactam; BP: benzylpenicillin; Clav: clavulanic acid; F: female; hyper: hypersensitivity; IDT: intradermal test; M: male; MD: minor determinant; ND: not done; P: patient; PPL: penicilloyl-polylysine; PV: penicillin V; SPT: skin prick test

**Table E2.** CD4+/CD8+ phenotype of drug-specific T-cell clones derived from blood of hypersensitivity patients to AX or Clav. Results analyzed by flow cytometry.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **AX-specific T-cell clones** | | | | **Clav-specific T-cell clones** | | | |
|  | **ID** | **n** | **CD4+** | **CD8+** | **CD4+CD8+** | **n** | **CD4+** | **CD8+** | **CD4+CD8+** |
| **AX hypers**  **patients** | **P1** | 17 | 10  (58.8%) | 5  (29.4%) | 0  (0.0%) | 14 | 11  (78.6%) | 1  (7.1%) | 0  (0.0%) |
| **P2** | 12 | 9  (75.0%) | 2  (16.7%) | 1  (8.3%) | 10 | 9  (90.0%) | 0  (0.0%) | 0  (0.0%) |
| **P3** | 16 | 13  (81.3%) | 2  (12.5%) | 1  (6.2%) | 7 | 2  (28.6%) | 4  (57.1%) | 0  (0.0%) |
| **P4** | 8 | 8  (100.0%) | 0  (0.0%) | 0  (0.0%) | 3 | 3  (100.0%) | 0  (0.0%) | 0  (0.0%) |
| **Clav hypers patients** | **P5** | 9 | 8  (88.9%) | 0  (0.0%) | 0  (0.0%) | 13 | 10  (76.9%) | 3  (23.1%) | 0  (0.0%) |
| **P6** | 14 | 5  (35.7%) | 7  (50.0%) | 0  (0.0%) | 16 | 8  (50.0%) | 6  (37.5%) | 0  (0.0%) |
| **P7** | 3 | 2  (66.7%) | 0  (0.0%) | 0  (0.0%) | 27 | 22  (81.5%) | 1  (3.7%) | 0  (0.0%) |

AX: amoxicillin; Clav: clavulanic acid; Hyper: hypersensitivity

**Figure E1.** Generation of AX- and Clav-specific T-cell clones derived from blood of hypersensitivity patients to AX (**E1A**) and Clav (**E1B**). Approximately 3,100 individual T-cell clones were generated cultured with autologous APCs and either AX or Clav for 2 days. Proliferation was measured by the addition of [3H]-thymidine. Results are expressed as stimulation index (SI), calculated by dividing the mean counts per minute (cpm) of drug-stimulated cells by the mean cpm of non-stimulated cells. Results were considered positive if SI > 1.5.

**Figure E2.** CD4+/CD8+ phenotype of drug-responsive T-cell clones derived from blood of hypersensitivity patients to AX or Clav. CD4+/CD8+ phenotype was analyzed by using flow cytometry. Box plots show medians of percentage of T-cells clones, with error bars showing 1st/99th percentiles. Statistical analysis was performed using Wilcoxon test (significant differences if P<0.05).

**Figure E3.** Profile of cytokines secreted by CD4+ AX- and Clav-specific T-cell clones derived from blood of hypersensitivity patients. T-cell clones were cultured with irradiated APCs and AX or Clav, and secreted cytokines were quantified and visualized by ELISpot. Images from seven representative AX- and Clav-specific T-cell clones.

**Figure E4.** Chemokine receptor expression on AX- and Clav-specific T-cell clones derived from blood of hypersensitivity patients. Results were analyzed by flow cytometry and expressed as median with error bars showing 1st/99th percentiles, and statistical analysis was performed using Mann-Whitney test (significant differences if P<0.05). \*\*\*P<0.001