Efficacy of dendritic cell generation for clinical use: recovery and purity of monocytes and mature dendritic cells after immunomagnetic sorting or adherence selection of CD14+ starting populations.

Abstract:
Immunotherapy with monocyte-derived dendritic cells (Mo-DCs) is applied to an increasing number of patients requiring large-scale production of clinical-grade dendritic cells with standardized Mo-DC generation protocols. In many countries, e.g., in Germany, Mo-DCs are legally considered medicinal products, which must be produced under Good Manufacturing Practice (GMP) conditions by an institution holding an official production license. Plastic adherence, immunomagnetic selection of CD14(+) monocytes and depletion of CD2(+) and CD19(+) cells are used to enrich monocytes for Mo-DC culture. The latter two have received approval of the European Union (CE). However, enrichment by plastic adherence is well-established and commonly used for clinical and research Mo-DC applications. The various plastic materials, nevertheless, have not been officially approved for monocyte selection for clinical use. In the present study therefore, we compared three methods for enrichment of CD14(+) monocytes with regard to efficiency of enrichment, yield of monocyte-derived functional mature dendritic cells, cost effectiveness, and handling. We demonstrate that CD14 selection and CD2 and CD19 depletion yield similar results regarding purity of mature DEs MoDCs (97-99% vs. 64-97%) and their immunostimulatory capacity. However, cell preparations cultured
after CD14 selection possessed 91% to 97% CD14(+) cells, whereas CD2-/and DC19-depleted preparations contained only 8% to 57% CD14(+) cells. Thus, positive selection requires smaller culture volumes to generate equal numbers of Mo-DCs. Both methods gave better results than plastic adherence. In conclusion, of the techniques examined, CD14 selection of monocytes gave the best results regarding reproducibility, yield, and purity of the resulting monocytes and mature Mo-DCs.