macrophages, as several scavenger receptors including SR-A1 expression is increased following to Leishmania infection [4]. Our investigations on J774 monocyte-macrophage cell line and murine bone marrow derived macrophages proved that polyanionic (succinylated and maleylated) branched chain polypeptides with poly[L-lysine] and their daunomycin conjugates were taken up by the cells via scavenger receptors [5, 6]. Here we report on the recent results of on the cellular uptake mechanism of ALK, the carrier of MTX conjugate with marked anti-leishmanial effect and structurally related polypeptides on murine bone marrow derived macrophages. Supported by a grant from the Hungarian National Research Fund (OTKA K104385). Rita Szabó is grateful for the MTA Postdoctoral Fellowship.


MOBILE GENOMIC ISLANDS: THE KEY ROLE OF EXTRACHROMOSOMAL AND INTEGRATIVE MOBILE ELEMENTS IN HORIZONTAL GENE TRANSFER

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The plasticity of bacterial genomes enables the rapid adaptation to the changing environmental conditions. Horizontal gene transfer (HGT), by which bacteria can acquire and disseminate many beneficial traits, is mainly responsible for this plasticity. Conjugative elements such as plasmids, some genomic islands (GIs) and transposons have a key role in HGT since their mobility can lead to the rapid acquisition of virulence, pathogenicity or resistance factors and/or complete metabolic pathways of bacteria. Recent investigations of bacterial genomes put the mobile GIs in the spotlight of scientific interest. Mobile GIs are classified into two groups: integrative/conjugative elements (ICEs) and mobilizable genomic islands (MGI). Unlike ICEs, MGIs are not self-transferable, so they require helper elements (ICEs or conjugative plasmids) that can provide the missing conjugal functions. GIs are stable part of the bacterial chromosome. They can not maintain extrachromosomally, but can be excised by site-specific recombination, transferred to other bacteria by conjugation and integrated into the chromosome of the recipient cell. These maintenance and transfer functions are encoded by the “backbone” of GIs, while another group of genes coding for antibiotic resistance, pathogenicity, catabolism pathways etc. confers adaptive functions to the host. The structure of mobile GIs shows remarkable flexibility: they evolve by acquisition, deletion and exchange of genes or gene clusters via homologous and/or site-specific recombination or transposition. One of the most studied MGIs is the Salmonella genomic island 1 (SGI1), which contains several antibiotic resistance genes embedded in the complex In104 integron segment. Prototype of SGI was detected in multiresistant Salmonella enterica serovar Typhimurium DT104 isolates, but its variants have also been identified in many other Salmonella serovars and in Proteus mirabilis isolates. Interestingly, SGI1 has never been found in natural Escherichia coli isolates even though it can easily be transferred into E. coli under laboratory conditions. SGI1 is a typical MGI, which is mobilized exclusively by the conjugative helper plasmids of IncA/C family. The first step of SGI1 transfer is the excision from the bacterial chromosome, which is carried out by the SGI1-
encoded site-specific recombinase Int and Xis. The induction of excision and the transfer process also requires helper plasmid-encoded functions.

Beside the conjugation apparatus (T4SS) of IncA/C plasmids, SGI1 also exploits regulatory functions of the helper plasmid. The plasmid-encoded FlhDC-family master regulator controls all conjugation genes of the plasmid including the relaxase, a key factor in the transfer initiation step, the operons of pilus assembly and perhaps some other functions. The master regulator triggers the excision of SGI1, i.e. signals the presence of a helper plasmid for SGI1, thus SGI1 hijacks both the regulation and the conjugation apparatus of IncA/C plasmids for its horizontal transfer. On the contrary, only SGI1 encoded functions are required for the integration into the recipient chromosome. SGI1 represents a good example how MGI s ensure their vertical transmission in absence of a helper and how they can exploit their helpers for horizontal spread.

**XMRV – A NEW RETROVIRUS**

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Recently the presence of a new retrovirus has been detected in prostate cancer (PCa) specimens and permanent PCa cell lines, exclusively in US laboratories. Sequencing showed its close relationship to Gammaretroviruses, especially mouse retroviruses. It was designated as “xenotropic murine retrovirus-related virus, XMRV” \(^1\). Infectious particles could be cultured in DU145 and LNCaP cells, the receptor (XPR1) also was identified. Electron microscopy showed typical C-type particles resembling Moloney murine leukemia virus (MoMuL). Viral polypeptides were visualised by using anti-MuLV antibodies. A unique 24 nucleotide deletion was shown in all isolates as compared to MuLV DG75. Isolates showed 98% nucleotide, and 99% amino acid homology, and high homology to MoMuL. Sites and other characteristics of integration were demonstrated in several PCa cultures and specimens, especially obtained in the hereditary forms with RNaseL and APOBEC A3G deficiency. Patients homozygous for RNaseL deficiency carried XMRV at the highest ratio (40%). Neutralising antibodies were shown in their serum. The rate of virus detection increased with the severity of Gleason score. Androgens, dexamethasone activate, IFN-b and some HIV integrase inhibitors block XMRV replication. XMRV was also detected in RNaseL deficient immune cells of patients with chronic fatigue syndrome. A publication error shed light on the problems in XMRV research. This virus was not detected outside US. Reagents used for other murine retrovirus studies resulted in false positivity in XMRV research. As retrospective studies showed, through maintenance of an XMRV negative prostate cancer specimen by serial passages in nude mice between 1992 and 1996, cells were contaminated by two endogenous retroviruses, subsequently their recombination occurred. The established permanent cell line, 22Rv1 already contained XMRV.

Its wide distribution among oncology and virology laboratories transmitted contamination to many other cell cultures. This case is an extremely important warning sign regarding biosafety practised in laboratories working with cell cultures and reagents of murine origin.

As XMRV can replicate in human cells, there is a high risk that through accidental infection or even a criminal case, it spreads to the human population causing an unknown disease.