

Chapter 2

Inheritance of Small Supernumerary Marker Chromosomes

2.1 De Novo and Familial sSMC

The rate of de novo compared with familial sSMC is approximately 70% and approximately 30%, respectively (Liehr and Weise 2007). That is, more than two thirds of sSMC evolve during gametogenesis or early embryogenesis (see Chap. 3), and the remainder have been passed at least from one generation to the next. The first report of an sSMC transmitted over three generations was by Ridler et al. (1970). For de novo sSMC it is important to know that the incidence of meiotic nondisjunction increases with advanced maternal age, whereas a similar effect was not observed in males (Schinzel 2001). Thus, prenatally, sSMC are often found in pregnancies studied because of advanced maternal age (Liehr 2011a).

For familial sSMC Dalprà et al. (2005) suggested that there could be a 2:1 ratio of maternally versus paternally derived sSMC, even though this suggestion aroused controversy. However, the suggestion was confirmed (Liehr 2006), and it is now known that sSMC are predominantly inherited via the maternal line (Table 2.1). Overall, a 1.8:1 ratio is present; as detailed in Table 2.1, this quotient is more expressed in sSMC derived from nonacrocentric chromosomes. In other words, acrocentric-derived sSMC tend to be transmitted more easily from one generation to the next than nonacrocentric ones; the first can apparently survive male and female meiosis more easily, whereas nonacrocentric ones seem to face more problems there.

Familial as well as de novo sSMC can be associated with fertility problems (see Sect. 1.2.2). This observation suggests evolutionary selection against aneuploidy caused by the presence of sSMC. This might be related to the reported selection against the additional X chromosome in males with a 47,XXY karyotype (Morel et al. 2000). On the basis of the observed predominant inheritance via the maternal line (Liehr 2006), in sSMC one of the main mechanisms during spermatogenesis could be selection of gametes without an additional extra chromosome (Manvelyan et al. 2008; Oracova et al. 2009). Evidence for this taking place was provided by the fact that any kind of chromosomal aberration (including sSMC) can reduce the

Table 2.1 sSMC frequency according to chromosomal origin and parental origin (data from Liehr 2011a)

Chromosome	Cases with inherited sSMC of		Ratio
	Maternal origin	Paternal origin	
1–12; 16–20; X, Y	37	14	2.6:1
13–15; 21–22	116	71	1.6:1
Sum of all chromosomes	153	85	1.8:1

ability of correct chromosomal pairing during meiosis I, which can cause fertility problems especially in males (Shah et al. 2003). In accordance with that, oligoasthenospermia and oligozoospermia are correlated with sSMC presence (Mau-Holzmann 2005; see Sect. 1.2.2).

Besides, selection against “sperm with sSMC” could also be driven in part via fertilization success. Problems in connection with sSMC replication arising predominantly in the more rapidly progressing sperm meiosis or a “weight effect” making sperm without an sSMC more rapid than those with an sSMC, similar to the effect known from Y-chromosome-carrying versus X-chromosome-carrying sperm (Smits et al. 2005), could be envisaged as possible mechanisms involved here.

Inherited sSMC are in general harmless; however, exceptions have been reported and should be considered as a rare possibility. First, there is the problem possibly caused by sSMC formed in connection with the McClintock mechanism (Baldwin et al. 2008; see Sect. 9.2.2). Second, loss of sSMC mosaicism can negatively influence the clinical outcome of an inherited sSMC. There are cases reported in which a paternally derived, seemingly harmless sSMC caused problems, as in the patient it was present in 100% of the cells, whereas in the father it was only present in a subset of his body (Anderlid et al. 2001, case I). Also an apparently harmless sSMC present in a parent in one copy may lead to problems in the offspring when the sSMC is duplicated there (Mears et al. 1995). Finally, very rarely, secondary rearrangements have been reported in an sSMC during transmission through generations, i.e., different sSMC shapes were reported in a mother and a daughter (Ing et al. 1987).

2.2 B Chromosomes and sSMC

B chromosomes are “additional passengers found in the karyotypes of about 15% of eukaryote species. They are best understood as genome parasites exploiting the host genome because of their transmissional advantage, and are frequently not deleterious for the organism carrying them” (Camacho 2004). B chromosomes have been described for plants, fungi, insects, crustaceans, fish, amphibians, reptiles, birds, and mammals, and are present in addition to the normal chromosome content, called A chromosomes. The evolution of B chromosomes depends mainly on two factors: transmission rate (i.e., drive) and effects on fitness. For old B chromosome

systems, it is plausible that they might have evolved toward neutrality (no drive or fitness effects), but it is thought unlikely that young extra chromosomes lacking drive or beneficial effects (even being neutral) might invade a population and become B chromosomes (Camacho et al. 1997).

Nonetheless, there are several similarities between sSMC and B chromosomes: both represent a heterogeneous collection of chromosomes added to the standard karyotype, both are small, both may consist of heterochromatic and/or euchromatic material (see Sect. 1.4.1), in both there is predominance of maternal transmission, and both demonstrate a tendency for mitotic instability (mosaicism; see Sect. 1.4.3). Most human sSMC seem to be evolutionary young elements, as their origin may be traced to another human chromosome through molecular analyses. Thus, according to current theories, sSMC would need drive, drift, or beneficial effects to increase in frequency in order to become B chromosomes (Liehr et al. 2008a).

Among sSMC there are at least two potential candidates that may already be or may evolve into B chromosomes: (1) sSMC stainable only by DNA derived from themselves (reviewed in Liehr et al. 2008a; see Sect. 6.25) and (2) acrocentric-derived inverted-duplication-shaped sSMC without an associated clinical phenotype (Liehr 2011a). As mentioned in Sect. 2.1, acrocentric-derived sSMC tend to be transmitted more easily through generations than nonacrocentric ones. Thus, there could possibly be a subset of familial acrocentric sSMC already behaving in a way similar to B chromosomes, and hence they could begin to spread in the population.

No definite B chromosomes have been described in humans. However, inverted duplicated derivatives of acrocentric chromosomes (especially from chromosome 15) fit the following prerequisites of B chromosome behavior: relatively high transmission rate, recurrent origin being predominantly neutral on fitness, and being on the way to a polymorphic status in the population. However, they have not yet acquired any differences in molecular nature in respect to A chromosomes. The latter is the main condition of the two cases of sSMC stainable only by DNA derived from them (see Sects. 6.25 and 7.25).

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